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SAJOUS'S
ANALYTIC CYCLOPEDIA
OF
PRACTICAL MEDICINE

BY
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SAJOUS'S
ANALYTIC CYCLOPEDIA
of PRACTICAL MEDICINE

D

DIABETES INSIPIDUS (POLYURIA).—DEFINITION.— Diabetes insipidus is a syndrome comprising several altogether dissimilar states, and characterized by marked increase in the quantity of urine, without any necessary qualitative changes in the elements of which it is composed.

ETIOLOGY.—While diabetes mellitus occurs most frequently in middle age, polyuria is not rare in childhood. One-half the cases start before the age of 35. In some families several polyurics may be found.

[In a case observed by Lauritzen, in a girl, 16 years old, four generations and 8 out of 19 members of the family had suffered from polyuria, viz.: the great-grandmother, 3 of her children, 3 grandchildren, and the great-grandchild,—the patient. The disease was, in all cases, directly inherited by the child from its parent, all the first-born being attacked. The great-grandfather suffered from enuresis, but not from polyuria. R. LÉPINE.]

Weil has reported the history of 4 generations of a family, including altogether 91 individuals, among which 23 suffered from diabetes insipidus.

In exceptional instances diabetes mellitus may be traced in the antecedents; much more frequently a neuropathic tendency is found. Predisposition is a most important factor in the etiology of this affection.

As for the determining or accidental causes, in a certain number of cases the polyuria is referable to a traumatic factor, *e.g.*, a fall upon the head. Sometimes diabetes mellitus immediately follows the traumatism and it is only after a time, two months or more, that a change to diabetes insipidus occurs. There is, consequently, an undoubted connection between the two affections. This has likewise been shown by experimentation. Claude Bernard, in puncturing a certain spot in the floor of the fourth ventricle in a rabbit, caused diabetes mellitus, while in puncturing at a slightly different point he caused simple polyuria. There is, however, always some degree of uncertainty in this result, and it is by no means true that experimenters can *at will* produce polyuria by puncture of the floor of the fourth ventricle.

After traumatism of the cranium, the chronic lesions of the encephalon, and tumors in particular, occupy an important place in the etiology of polyuria. I have seen several cases of this kind. In one of them there was found at the autopsy a tumor of the optic thalamus. The polyuria appeared very suddenly. The large size of the growth suggested that it might have compressed the pedicle of the pituitary. (See under Pathogenesis.)

Case of diabetes insipidus in a man of 56 years of age who presented during life the symptoms of a diabetes insipidus with, at times, a severe polyuria. At the autopsy, a chronic diffuse inflammation of the ependymal tissue was found at the base of the fourth ventricle. Karl Pichler (Zentralbl. f. innere Med., Aug. 1, 1913).

Case of diabetes insipidus in which there were symptoms pointing to a cerebral origin of the disease. A man, aged 43 years, had for four years the typical manifestations of diabetes insipidus. The urine varied in amount from 7500 to 11,000 c.c., and was always of low specific gravity, 1001. Lumbar puncture was made for the purpose of investigating the cause of the trouble. Less than 5 c.c. were withdrawn, the fluid escaping slowly under low pressure. Within forty-eight hours the daily amount of urine had dropped to 660 c.c. Headache, pain in the back of the neck, anorexia and vomiting, with a feeling of general weakness followed the puncture. Morphine was given for pain and almost no fluid or food was taken for three or four days. But after the prostration following the lumbar puncture had disappeared and when food and water were freely taken, there was no thirst, as before, and the amount of urine for a period of four weeks never exceeded 1800 c.c. for twenty-four hours. The specific gravity averaged 1015, ranging from 1005 to 1031 (single specimen). The result of the puncture suggests that the cause of the polyuria in this case was a lesion of the brain, perhaps in the pituitary. Herrick (Arch. Int. Med., vol. x, No. 1, 1912).

Syphilitic lesions of the encephalon are causes of polyuria.

Emotions and accidental causes also bear a relation to this affection.

Finally, the abuse of alcoholic beverages is a frequent cause of diabetes insipidus.

In children, one-tenth of the cases of diabetes insipidus have been observed to be preceded by some infectious disease.

The following will give an idea of the relative frequency of the different causes operating to produce diabetes insipidus:—

Heredity	10
Neuropathic disposition	20
Trauma of the skull, organic lesions of the encephalon (including syphilitic lesions)	30
Excesses of all kinds	15
Various accidental causes, including infectious diseases	25
	100

PATHOGENESIS.—Eckhard has, of all physiologists, been the most energetic in his advocacy of the hypothesis that there exist nerves which produce polyuria. In his experiments, indeed, he witnessed the occurrence of the latter after superficial excitation of the vermis, without any accompanying change in the aortic blood-pressure. Moreover, section of the splanchnic nerve is followed both by polyuria and lowered vascular tension.

As for the details of the mechanism through which there occurs in the kidney an increase of the excretion of urine, in cases where there is no primary dyscrasia and, in particular, no excess of water in the blood-stream, they are still shrouded in obscurity. The circulation through the glomeruli is known to be increased, and the possibility that this occurs owing to relaxation of the arterioles must be admitted. A relaxation of the *efferent* vessel may, in particular, be supposed to occur. If this be the case, the blood-pressure must increase in the capillary network which follows the glomerulus, and the mechanical conditions for the reabsorption of water are unfavorable to its occurrence. The benefit conferred by vasoconstricting remedies (see Treatment) tends to support the idea that vasomotor relaxation is an important factor in the production of polyuria.

In a few cases,—on the whole quite rare,—polydipsia appears to be the initial manifestation of the disease. In one case the patient was observed to develop an *intense thirst* as the initial symptom after a fall on the head. Such observations as these lend support to the idea that there exists a *nervous* form of thirst. They are exceptional, however.

The important rôle played by disturbances of the internal secretions in the pathogenesis of many diseases, and, in particular, of diabetes mellitus, is well known. Sufficient information on this subject is supplied in the works of Sajous, to which I refer the reader. It is not impossible, moreover, that the original cause of certain cases of diabetes insipidus is to be found in an excessive secretion on the part of the hypophysis. Certain observations tend to justify this view and would even appear to be paving the way to its definite demonstration. Particularly interesting in this connection is Simmond's case, in which an effort to localize the source of the disorder led to the *pars intermedia* of the pituitary body as a source of polyuria.

> Case of a woman of 37 who developed intense polyuria two months after removal of a cancer in the breast, the amount of urine varying from 10 to 19 liters a day. Necropsy three months after the operation showed that the entire posterior portion of the hypophysis had been entirely destroyed by a metastatic cancerous process. Consequently, the polyuria could not have been induced by the secretion from this portion of the hypophysis. Schäfer's research has established that the anterior portion of the hypophysis can have nothing to do with the secretion of the urine. The intermediate portion, although intact, yet must have been irritated to hyperfunctioning by the adjacent destructive process in the posterior portion. That this *pars intermedia* is responsible for diabetes insipidus, is thus rendered probable. Simmonds (Münch. med. Woch., Jan. 21, 1913).

In a case reported by Stuber (Deutsches Archiv für klinische Medizin, vol. civ, p. 394) diabetes appeared quite suddenly without apparent cause in a man 48 years of age. The blood appeared to contain an excess of epinephrin.

[Sajous has held several years that the adrenals and the kidneys were governed by sympathetic nerves originating in the pituitary body, which in his opinion contains the sympathetic center, and that irritation of this center caused concomitant overactivity of the kidneys and adrenals.]

SYMPTOMS.—The malady may begin insidiously; but it is not unusual for it to appear suddenly, either following one of the causes which we shall name later on, or even without any appreciable cause. It may, in exceptional cases, manifest itself during childhood or infancy.

[I have had under observation a young man 16 years old who was subject to excessive thirst since the first months in his life, the first word he pronounced, at the age of 8 months, being *"water."* R. LÉPINE.]

> Case of a girl aged 8 years, who suddenly developed polyuria, the urine not containing sugar. She gradually failed, and fifteen days later symptoms of coma appeared, which proved fatal in three

days. The pulse was feeble and compressible, and the respirations increased in frequency and sighing. The temperature never rose above normal. Carter (Lancet, Aug. 27, 1904).

Case of diabetes insipidus under observation for twelve and one-half years. The disease seemed not to have been congenital, but to have arisen when he was only 3½ years old, and to have followed an attack of measles, complicated by laryngitis and otitis media, which left him delicate and with a suppurating middle ear. He remained diminutive in stature (his twin brother was nearly 6 feet high and he was only 5 feet 4 inches) and with a high-pitched, feminine voice. The necessity for holding large quantities of water gradually led to a greatly increased capacity of his bladder, and when first seen, at 13 years of age, it reached to his umbilicus and contained 45 ounces by measurement, and that was only incidental, and not an experiment to determine how much it could possibly contain. Verco (Austral. Med. Gaz., Oct., 1909).

Thirst and polyuria are the predominating symptoms of the affection. The urine is abundant, usually very pale in color, and is slightly acid. Its specific gravity varies from 1002 to 1010. Consequently, the organic and inorganic principles are not present in any great quantity, but, taking into account the daily amount of urine, it will be found in a certain number of cases that the total quantity of organic and inorganic substances usually considerably exceeds the normal average. With regard to the relative proportions, the chlorides are increased.

In inducing unilateral polyuria in a dog, for instance, by severing a splanchnic nerve, I have thus observed relative increase of the chlorides.

The quantity of urine voided during the twenty-four hours naturally bears a certain relation to the quantity of fluid ingested. As the cutaneous perspiration is usually greatly diminished in diabetic patients, there is, as a rule, less difference between the quantity of fluid taken and that of the urine than in the normal state.

It is even possible that, in exceptional cases, the quantity of fluid taken in one day may be less than that of the urine voided during the same period of time.

In explanation of this paradox there are three hypotheses:—

The first (which is the most natural) is the supposition that during this period the organism becomes impoverished as to water. This hypothesis agrees with several conditions sometimes noticed in polyuric subjects, particularly the increased density of the blood; in this case the weight of the patient should be less during the period in question.

The second hypothesis, which, though not based on any positive fact, does not seem irrational, premises that there is a much greater formation of water in the economy than under normal conditions. In this case, there should be a diminution in the respiratory quotient $\frac{CO_2}{O}$. If there is more water formed, there is less CO_2 exhaled. It has been estimated that in a polyphagic individual 100 to 200 Gm. (3⅓ to 6⅔ ounces) of water may be produced in the twenty-four hours in this way.

The third hypothesis appears to be less plausible. It consists in the supposition that the economy may absorb, particularly through the lungs, a certain amount of water vapor. It is well known that in the healthy subject copious ingestion of water is followed, during the two consecutive hours, by the loss in the urine of the greater part of the water taken. This is not the case in diabetes insipidus; the elimination is less rapid, either because the kidney has partially lost its functional elasticity, which enabled it in the normal state to free the blood from an excess of water, or rather because the economy, being, relatively speaking, deprived of water, takes up a certain portion of that ingested.

In the same connection it may be noted that in the polyuric subject the difference existing in the healthy person between the urine secreted in the twelve hours of the day and that of the night is not noticeable.

In a few cases of diabetes insipidus —naturally, the most grave ones—it has been observed that the ingestion of a large amount of sodium chloride does not increase the concentration of the urine. The only effect produced is an augmented urinary output, owing to the excretion of a larger quantity of water. These cases are thus characterized by an *inaptitude to concentration of the urine*, even though there be an excess of salts in the blood. Such cases are, however, rather rare.

Falck advanced the opinion that absorption is retarded in polyuric patients. This supposition is, on the whole, not very likely, but I would say that the dilatation of the stomach sometimes observed in such patients might confirm it in certain instances.

Thirst is a very marked symptom, which, in certain exceptional cases classed under the head of polydipsia, is the original symptom. This point will be again referred to under the head of Diagnosis.

The digestive function is impaired in polyuric patients. This is readily understood, the digestion being disturbed by the ingestion of a large quantity of water, which dilutes the gastric juice. Constipation usually exists.

The sudatory function is almost always abolished. In several patients the fact has been noticed that pilocarpine is incapable of bringing about sweating. Owing to this inability to perspire, it sometimes happens that during great heat in the summer the temperature of these patients rises to 38.5° C. (101.3° F.) and even to 39° C. (102.2° F.). This hyperthermia is not accompanied by malaise.

The insensible perspiration is nearly always greatly diminished,—most frequently reduced to one-half the normal amount,—but sometimes almost abolished. This contributes to the explanation of the fact, already referred to, that the patient excretes as much fluid as he ingests.

Exceptionally, patients have been observed to show copious sweating. The occurrence of this is accompanied by a subjective sense of betterment in the general condition.

An equally interesting phenomenon which has been noticed in a very few cases is an abnormal flow of saliva. Külz observed this complication for a time in a young hysterical subject, and was able to collect, in one day, more than 1 pint of saliva. It is known that physiologists have, during their experiments, sometimes observed salivation in dogs after lesions of the medulla oblongata, etc. In some cases the pulse is slow, and there is also a certain relation between this slowness of the pulse and the increase of the polyuria.

The blood is sometimes *more concentrated* than in the normal state, but this is a quite exceptional symptom.

COMPLICATIONS. — Complications referable to the nervous system are often met with in cases where the polyuria is itself of nervous origin. These morbid phenomena are merely concomitant, not depending upon the polyuria, but upon its cause. Such manifestations are, *e.g.*, headache, vertigo, neuralgic pains, vomiting, etc. As partly dependent, on the other hand, upon the polyuria may be considered such nutritive disturbances as find their expression in emaciation, coming on even though the patient is polyphagic. It is certain that the excessive washing out to which the tissues are subjected is a cause of exaggerated waste. The presence of inosite in the urine has occasionally been observed. This has been explained as being the result of excessive flushing out of the organism.

DIAGNOSIS.—This usually presents very little difficulty. The absence of abnormal principles in the urine indicates by exclusion the existence of simple polyuria. It may happen, however, that the diagnosis between this condition and that of interstitial nephritis gives some little trouble. In certain cases of the last-named affection albuminuria may not exist during a certain period. On the other hand, there are cases of polyuria in which, without any actual nephritis, traces of albumin may be found in the urine.

However, when interstitial nephritis exists, certain uremic symptoms, hypertrophy of the heart or some one of the symptoms of Bright's disease, are always present. Besides searching for the symptoms of uremia (cephalalgia, dyspnea, etc.), it should also be remembered that a patient suffering from Bright's disease retains nitrogen in his blood—a fact readily established by ascertaining the quantity of nitrogen in the serum after the albumin has been precipitated—and eliminates less nitrogen in his urine than polyuric patients, and that the urine frequently contains casts. In view of these characteristics, it is generally easy to establish a diagnosis.

How is primary polyuria to be distinguished from primary polydipsia?

In polydipsia thirst is unquestionably the first symptom; it is not preceded by frequent micturition. Polyuric patients do not perspire; in polydipsia perspiration is likely to occur. In the latter affection the quantity of urine does not equal the quantity of liquid ingested; so that, if the patient refrains from drinking during several hours, there will be during this time a diminution or even an arrest of the excretion of urine.

> True diabetes insipidus can be differentiated from primary polydipsia by the behavior after increased intake of salts. Patients with primary polydipsia display the normal power of eliminating a concentrated urine under these circumstances, which is not the case in diabetes insipidus. The latter is further distinguished by the fact that while it shares with interstitial and pyelitic processes the inability to produce a concentrated urine, yet the amount of concentration of the latter is much more constant and the substances in solution are eliminated much more promptly and more regularly. Theocin has the effect of raising the concentration in diabetes insipidus without increasing the amount of urine. Phosphoric acid ingested in the form of sodium phosphate is eliminated in both normal conditions and in diabetes insipidus without increasing the amount of urine. E. Meyer (Deut.

Archiv f. klin. Med., Bd. lxxxiii, Nu. 1-2, 1905).

TREATMENT. — In neuropathic subjects the general condition should be treated by means of **bromide of potassium, valerian,** and especially by **strychnine,** which has yielded very gratifying and successful results.

Case in a man of 49 years, who developed diabetes after a fall which resulted in a severe shock to the nervous system. The writer tried various methods of treatment without success, until he began the injection of **strychnine,** as recommended by Feilchenfeld. The nitrate was given in daily quantities of from 0.0025 to 0.005 Gms. (1⁄25 to 1⁄12 grain) for twenty days. The urine, which had amounted to 8000 c.c., continued to steadily decrease in amount. The drug had to be stopped at the end of twenty days, on account of the symptoms of intoxication, but the urine continued to decrease in amount down to 2400 c.c. The patient's general condition also improved and at the end of four weeks the urine was about 2000 c.c. daily and the man was practically cured. No explanation of the action of the drug in this case is offered. B. Leick (Deut. med. Woch., Aug. 11, 1904).

Different therapeutic measures gave the following results: Change in diet did not decrease the amount of urine, while it made the patient very uncomfortable. Decreasing the amount of fluid ingested was also a failure, since severe nausea, vertigo, and weak pulse were the result and the amount of urine dropped only from 10 to 8 liters. Cold baths were refreshing, but warm water, applied in the hopes of stimulating diaphoresis, was not borne well. Preparations of valerian, large doses of antipyrin, the bromides, arsenic, sodium cacodylate, mercury, and the iodides did not make a lasting impression upon the disease, but good results were finally seen from small, gradually increasing doses of **strychnine,** injected subcutaneously. Polyuria and polydipsia disappeared in three weeks and the patient rapidly gained in weight. B. Stein (Münch. med. Woch., Sept. 6, 1904).

While treating a man aged 60 years for vesical paralysis by means of hypodermic injections of **strychnine,** Feilchenfeld noticed that the treatment caused a practical cure of the polyuria, with which the patient was also affected. He also treated with success a second patient suffering from simple polyuria in the same manner. The writer has also had recourse to the same mode of treatment in four instances of diabetes insipidus. In three of these, recovery resulted. The quantity of urine which had been from 9 to 11 quarts in the twenty-four hours was diminished to from 2 to 3 quarts, and in two of the patients the specific gravity returned to normal. The beginning dose was 1⁄120 grain (0.0005 Gm.); this was gradually increased. L. de Ketly (Semaine méd., p. 282, 1906).

Case of diabetes insipidus developing after an injury to the head and favorably influenced by **strychnine.** The trauma must have affected the vasomotor centers governing the circulation in the kidney, with the diabetes as the result. The strychnine had favorably modified the centers in question, and thus indirectly it had benefited the diabetes insipidus. Spaether (Berl. klin. Woch., Bd. xliii, Nu. 29, 1906).

For the special treatment of the polyuria **ergot** of rye (or, even better, **ergotine**) and **antipyrin** should be used.

Case of diabetes insipidus in a child aged 4 successfully treated by **atropine.** Before treatment the child was drinking every quarter of an hour and getting no proper sleep. About 9 liters of fluid were taken in the twenty-four hours, and 7 to 8½ liters of pale urine of specific gravity 1002 to 1006 was passed. There were no albumin, no sugar, and no abnormal elements present in the urine. The skin was very dry and abdomen swollen. On January 11th the atropine treatment was commenced, and continued until March. The drug was given by the mouth in a solution of 1 grain (0.065 Gm.) to 10 grains (2½ drams) of water. Of this solution 1 drop (0.06 c.c.), increasing to 18 drops (1.08 c.c.) per diem, was given daily. No ill effects were observed beyond a slight skin eruption in the early days. At the end of the treatment the child only drank 1½ liters as against 9, and the urine passed only reached 1200 to 1400 c.c., and the specific gravity increased to 1010 to 1013. Fontana (Gaz. degli osped., May 12, 1907).

Case of a man 29 years old, syphilitic for five years, who suddenly became affected with excessive thirst and polyuria; four months later the patient had become markedly cachectic and the urinary conditions persisted in spite of ordinary treatment. At this time the hypodermic administration of **mercury protiodide,** ¾ grain (0.048 Gm.) daily, was begun, in connection with the internal administration of **potassium iodide** in doses of 30 grains (2 Gm.) daily. After two months of treatment the patient was completely cured. Vaphiades (Revue de méd., iii, 296, 1907).

Case of diabetes insipidus in which both malaria and syphilis were traced, the prompt improvement under mercurial treatment confirming its syphilitic nature. The benefit has not been stable to date; the polyuria returns when treatment is suspended. In the literature on the subject, both **mercury** and **iodide** are stated to have been effectual. X. Arnozan (Jour. de méd. de Bordeaux, March 17, 1912).

I have obtained some success by the use of the **continuous current,** the positive pole being placed upon the spinal column, and the negative at the level of the hilum of the kidney.

When patients are able to stand without too much distress a limitation of the intake of **fluid,** this **restriction** should be imposed; it should be kept in mind, however, that in the grave cases it is absolutely impossible of realization.

In a few cases some degree of betterment has been experienced through the use of **diaphoretic measures.**

Lumbar puncture has occasionally been resorted to, but the results so far have not been conclusive.

R. LÉPINE,
Lyons.

DIABETES MELLITUS.—

DEFINITION.—A malady characterized by non-accidental—that is to say, a permanent or very nearly permanent—glycosuria.

ETIOLOGY.—The incidence of diabetes varies to a great extent in accordance with the factors of age, race, occupation, etc. It is not the same in different countries. All that can be said, in a general way, is that diabetes is not a rare affection. The statistics put forth by Williamson show, indeed, that different countries are very unequally afflicted with it. Among the different cities of France there is a singular divergence in the incidence of diabetes; thus, by comparison with Bordeaux, the disease is relatively rare in Lyons. The number of cases does not appear to be increasing in the last-named city, whereas in Berlin it is showing a constant progression. In Paris, according to Bertillon, after a period of rapid increase, the increment since 1890 has been very slight.

The mortality from diabetes per 100,000 inhabitants ranges from 6.6 to 12.7 in the different cities of England and Wales, with a general average for the country of 9.6; in Malta and Gozo, 37.8. In Europe the extremes are 5 in Helsingfors, 4.5 in Italy to 15.8 in Copenhagen, 20 in Berlin, and 25.8 in Bordeaux; in Asia, from 0.15 in Hong Kong to 9.2 in Calcutta; in America, from 5.8 in the province of Quebec to 27.3 in Worcester, Mass., with 17.4 in New York, 10.7 in Chicago, and 17.9 in

Boston, and a general average for the United States of 13.9; for Australia, of about 8; for Buenos Aires, 5.6, and Cuba 2.8. The author's research shows that the disease is gradually increasing. Williamson (Münch. med. Woch., Oct. 12, 1909).

The relative frequency of diabetes mellitus in middle age and in the period of decline is well known. Below the age of 30, on the other hand, and especially in childhood, it is relatively quite rare. The dominant cause of diabetes in childhood is an inherited tendency.

Men are much more likely to be attacked by diabetes than women. Cantani reported that, out of 1004 cases, 837, or 83.37 per cent., were males, and 167, or 16.63 per cent., were females. This difference is, however, somewhat excessive and is not reproduced in other statistics.

The proportion of males and females in the white race who suffer from diabetes is about 3 to 2. In children, however, the ratio is not the same; girls have it somewhat more frequently than boys. According to Futcher, in the colored race the cases occur more frequently in women than in men. In the same country different races are very unequally affected, and on this point, too, it is necessary to await further investigations.

The prevailing belief at the present time is that diabetes occurs with relative frequency in the Jewish race. Wallach found that, out of 156 persons who died from diabetes, 51 were Jews and 105 belonged to other denominations. The mortality from diabetes is six times as great (according to this author) among Jews as it is in other religions. The correctness of this conclusion has, however, been challenged by Pollatschek.

Statements concerning the morbidity of Jews in relation to diabetes mellitus are of little value, as there is never any statement as to the relative number of Jews and Christians in the clientele of the reporter. The writer treated 4714 persons, 2381 of whom were Christians and 2333 Jews. There were 653 diabetes, 289 of these being Christians and 364 Jews; *i.e.*, reckoned by the number per thousand of all patients, 124 Christians and 155 Jews had diabetes. Moreover, diabetes is common in England, where there are few Jews. Pollatschek (Zeit. f. klin. Med., Bd. xlii, Hft. 5-6, 1901).

H. Stern states that 202 deaths from diabetes in the city of New York during 1899 showed that the greatest mortality occurred between the 55th and 65th years, and diminished rapidly toward the end and beginning of life; 57 were born in Germany, 51 in United States, and 37 in Ireland. At least 54, or 25 per cent., were Jews and 51 were Irish.

Diabetes is frequently hereditary, inasmuch as several members of one and the same family are often affected.

Family with eight children, all apparently robust, until one after the other five of the children died between the ages of 4 and 11 of typical diabetes mellitus. The environment was good and the children well cared for, but five died from the disease in the course of nine years. No lesions were found *post mortem* in the first child that died, but in the last child the pancreas was markedly degenerated; no necropsy was obtained in the others. Langaker (Deut. med. Woch., Feb. 2, 1911).

The influence of heredity is much greater than that of race,—a fact which is not surprising, the component units of a race being much less like to one another than those of a single family. The factor of inheritance is observable in one-fifth of all cases. That which is inherited, however, is not so much the disease itself as the predisposition to it, since rather frequently diabetes appears in the offspring before it has become manifest in the father.

The hereditary form of diabetes is seen as often in women as in men. Among 1000 cases, 790 were in Jews, and the most frequent age was from 50 to 60 years. The disease most often appears in persons previously healthy and well nourished, but frequently neuropathic. The course is generally mild and often combined with arteriosclerosis, less often with pulmonary tuberculosis. Death is usually due to some intercurrent disease. The hereditary form of the disease appears to be of nervous origin rather than due to pancreatic disease. M. Loeb (Zentralbl. f. innere Med., Aug. 12, 1905).

Frerichs found that in 10 per cent. of 400 cases of diabetes an inherited predisposition could be incriminated; Külz, 25 per cent. in 592 cases; Naunyn, 17 per cent. in 398; von Noorden and Williamson, about the same percentage; Schmitz found a history of diabetes in other members of the family in 47 per cent. of 2115 cases. The family history of 100 diabetic and 100 other hospital patients of the same class studied by the writer showed only 7 relatives with diabetes among the 100 non-diabetics, while the corresponding number among the 100 diabetics was 18. The diabetes had commenced before the age of 10 in 7 of the 100 cases and in 18 between 10 and 20. In 90 per cent. no cause for the diabetes was known; on the others there was cirrhosis of the liver or lithiasis. K. A. Heiberg (Hospitalstidende, March 20, 1912).

It has been justly remarked that these diabetic families are tainted with the uric acid diathesis, and that obesity, gout, and neuropathic affections exist in extraordinary frequency in such families (Prout, Bence-Jones, Bouchard). Frequently obesity and diabetes coexist in the same person. A too abundant diet and the abuse of wine and cider are predisposing causes of diabetes. In 607 persons engaged in manual labor or requiring great muscular and respiratory activity whose urine was examined by Worms, no sugar was found in any case; in 100 persons engaged in intense itellectual work, sugar was found in 10, a proportion which appears to me exaggerated.

The causes which we have mentioned so far are *predisposing* causes.

Determining Causes.—As to the *efficient* causes of diabetes, acute infectious diseases can be considered in this category, for the affection sometimes comes on after typhoid fever, eruptive fevers, etc., and especially after influenza. With regard to malaria, several French physicians have noted a temporary glycosuria after attacks of intermittent fever; but in malarial countries true diabetes does not appear to be any more common than elsewhere. The importance of syphilis has also been exaggerated.

The part played by contagion in diabetes is as yet not based upon any very exact observations. The occurrence, said to be quite frequent, of diabetes in husband and wife has been a mooted question. An analysis of 2320 cases by Schmitz gave 26 examples of such occurrence, probably mere coincidences, as believed by Senator.

[A feature which is overlooked in this connection is that the same diet is partaken of by husband and wife. In two of Sajous's cases the excessive use of sugar and sweets caused the glycosuria. If, as he states, their mates had also acquired the habit, each couple would have been characterized as suffering from conjugal diabetes in statistical tables, suggesting contagion—obviously an erroneous conclusion.]

The writer found 5 cases of diabetes in both man and wife among 25 diabetics, and Debove 6 cases among 50. This is a far larger proportion than that mentioned by Schmitz and Deléage, who noted only 1.12 and 3.55 per cent. among 2320 and 478 cases of diabetes, respectively. The discrepancy in the statistics is due to the fact that the latter physicians practise in watering places, where they see the patients only for a short time and know little of their family life. Martinet (Presse méd., Dec. 7, 1904).

Examples which suggest possible transmission. A case in a woman whose husband's brother and his wife both had the disease; also a case developing in a man after marrying into a diabetic family, both parents of his wife having diabetes. In another case, a physician, 42 years old, developed diabetes not long after he had amputated, in another town, the leg of a patient on account of diabetic gangrene. There were also in the same street with the diabetic physician four other men with diabetes, one of whom had a diabetic wife. Six cases of diabetes in a town of only 2500 people, and all among close friends and neighbors, one of whom kept a saloon frequented by the others, is certainly a remarkable coincidence. In the writer's own experience he found the husband or wife also affected in 22 cases among 516 married patients with this disease. From this list he subtracts 3 cases in which the diabetes developed in both simultaneously after some great emotion, such as the burning or death of a child. In the 19 cases of conjugal diabetes an interval ranging from 1 to over 15 years elapsed between the development of the diabetes in the second party, the couples having all been married for from 23 to 42 years. Senator (Berl. klin. Woch., Jan. 27, 1908).

Diabetes mellitus, as suggested by the writer in 1909, is an infectious disease, due to the presence in the blood of the yeast fungus, *Saccharomyces cerevisiæ*, This fungus is found in all diabetic urine; a pure culture was obtained of it from the blood of every case the writer examined, 40 in number; the opsonic index or resisting power of each patient varied with the physical condition from 0.46 to above 1, or normal; by the use of a vaccine this opsonic index was increased and all symptoms of diabetes relieved. Alfred King (Monthly Cyclo., July, 1910).

Mental shocks, violent emotions, especially of fear, may be the cause of diabetes. Smith and others have emphasized the frequency with which this affection occurs in locomotive engineers. In addition to pronounced emotional stresses and prolonged worry, especially financial worriment, grief, such as follows, for example, the loss of a child, also unquestionably exerts a diabetogenic influence in predisposed individuals. According to statistical studies of the question, these various causes are operative in at least one-third of the cases of diabetes.

A number of cases are reported in the literature in which diabetes has followed a shock or psychical trauma. For the most part these cases have not been severe, but in the two reported by the author both died. Lorand (St. Petersburger med. Woch., May 31, 1903).

While the relative mortality from diabetes during the past ten years among all employés of the Paris, Lyons and Mediterranean Railway Company has been 3 per mille, that among the stationary employés was only 1.76 per mille, and that among the travelling *personnel,* 13.10 per mille for guards and carriage attendants, and 12.63 per mille for drivers and stokers. The writer attributes the preponderance in the ratio among the latter classes to *vibration,* and utters a warning note to automobilists who constantly subject themselves to similar vibration. Navarre (Semaine méd., Nov. 15, 1905).

Many other etiological factors might be mentioned. Thus in some instances diabetes is observed to appear during pregnancy or after the early cessation of lactation. Cases have been reported, on the other hand, in which the phenomena of the disease ceased during a part at least of the gestation period. These various occurrences may be fairly well accounted for when one tries to analyze them. Thus, in the last-mentioned instance, it is with women whose nutritional processes have been slowed and who were eating to excess that one has to deal. The growth of the fetus has been of benefit to them in that it eliminated for them an excess of nutritive material.

Traumatic Diabetes.—According to my personal statistics, 5 out of every 100 diabetics have been the victims of trauma. Cantani would place the ratio at twice that mentioned, but in my opinion such an assertion is greatly exaggerated, especially in the adult. Perhaps it can be sustained, however, in children, since falls on the head are very common among them. Trauma of the skull is, indeed, particularly effective as a cause. It must be clearly kept in mind, however, that the knowledge of a previous traumatism does not necessarily imply that the diabetes present is of traumatic origin, for in a certain number of these patients the existence of an inherited predisposition may be noted. In such instances traumatism acts only as an accidental cause.

A study of 212 cases of traumatism of the head admitted into the Boston City Hospital within thirteen months. Ranged in 5 classes: (1) wounds of the scalp; (2) wounds with denudation of the bone; (3) commotion, including cases followed by loss of consciousness, but without fracture; (4) fracture of the vault; (5) fracture of the base. F. A. Higgins and J. B. Ogden found that of the first class there were 84 cases, 5 of which, or 6 per cent., presented glycosuria; in the second class, 43 cases, 4 with glycosuria,—9 per cent.; third class, 40 cases, 1 with glycosuria,—2.5 per cent.; fourth class, 24 cases, 5 with glycosuria,—20.8 per cent.; fifth class, 21 cases, 5 with glycosuria,—23.8 per cent. In all there has been 20 cases of glycosuria in 212 cases.

Among 100 cases of traumatic diabetes a more or less severe lesion of the floor of the fourth ventricle was found in approximately 25 cases, various lesions of the central nervous system in 40, and no discernible lesion in 35.

Through the advances being made in anatomical studies, the last of these categories will doubtless be further reduced. This is all the more probable since, in the absence of all trauma, violent emotion in itself appears to be sufficient to produce a slight lesion (through vasomotor action). Thus, Williamson reports the case of a healthy young woman who, upon witnessing her nephew sustain a fall, experienced an extreme emotional shock, then remained in a state of anxiety which rendered her incapable of all work. Four weeks later polyuria and glycosuria were observed; then symptoms of grave diabetes, from which she succumbed in seventeen months. The autopsy revealed the presence of small hemorrhages in the floor of the fourth ventricle.

Independently of traumatism, there are sometimes found in diabetics, though rather uncommonly, lesions of the nervous system. The number of unquestionable reported cases of spontaneous lesions of the fourth ventricle which had brought on diabetes does not exceed about 15.

As for the organic changes (softening, etc.) which may be found in the cerebral hemispheres in diabetics, it is not permissible, without further information, to assert definitely that they are the cause of the diabetes. In a certain number of cases proof is available of the fact that they are secondary.

Lesions of the Liver.—Owing to the views of Claude Bernard, much attention has been given to the condition of the liver in diabetes. In most instances, however, this organ has been found normal *post mortem;* in one-third of the cases, slightly enlarged.

In rare instances a more or less cirrhotic state of the liver is discovered. When this condition is present, microscopic examination shows that the pancreas is also cirrhotic; the production of this has been explained on the basis of abnormal pressure in the portal system.

Hanot and Chauffard, Letulle, and others have called attention to the possible simultaneous presence—which is, however, rare—of a cirrhosis of the liver, generally hypertrophic, of a more or less generalized pigmentation, and of diabetes. To this combination of phenomena has been applied the term *bronzed diabetes.* Is this an especial form of diabetes? It would be somewhat premature to give a positive answer, for the diabetes designated as "bronzed" might be merely a complication of pigmentation, itself the result of a hemolytic process, and which gives rise to diabetes in cases where cirrhosis of the pancreas is developed.

Lesions of the Pancreas.—A more or less marked cirrhosis of the pancreas is met with in a large number of individuals, whether diabetic or not. If this process is to exercise any noteworthy pathogenic influence, it must be of a certain degree of intensity, and the atrophy of the organ must be very pronounced. Such a condition presents itself in approximately one-half of all cases of calculous pancreatitis, which is, of course, an uncommon affection.

Carnot had laid stress on infection by the ascending route as a cause of pancreatitis; but the frequency of this route of infection is at present contested (Richet, Jr.).

It is quite out of the question to gain an exact appreciation of the etiological value of a pancreatic lesion with the naked eye alone. A histological examination is indispensable, for the microscope alone will permit of distinguishing the common pathological change, periacinous cirrhosis, from intra-acinous cirrhosis, which process alone offers an obstruction to the elaboration of the internal secretion of the organ.

Importance of the Pancreatic Internal Secretion.—That a gland possessed of an excretory duct should also elaborate an internal secretion need occasion no surprise. As Brown-Séquard said, all tissues yield up *something* to the lymph and venous blood, especially tissues and organs whose functional activity is very great. The pancreas, among organs, is quite especially distinguished in this direction. Its temperature, at least at certain times during the period of digestion, is the highest occurring in the entire body (R. Lépine: Arch. de méd. expér., 1899, p. 543). There are therefore sound reasons for maintaining that this organ supplies an important internal secretion. On this subject, one should read, in particular, Chapter VIII of the first volume of either of the first four editions of Sajous's work on the "Internal Secretions." This chapter is of the greatest importance, and I shall refer the reader to it.

I do not believe in the specificity of the islets of Langerhans (see farther on), and was the first to assert the existence of a pancreatic internal secretion (Lyon méd., Dec. 29, 1889, and Rev. scientif., Feb. 28, 1891; see also Rev. de méd., May 10, 1910, p. 420).

> The authors' experiments seem to indicate that the pancreas normally produces a hormone which circulates in the blood, and the presence of which is necessary in order that the tissue cells may be able to assimilate and utilize the sugar of the blood. Absence of this hormone leads to glycosuria. Knowlton and Starling (Lancet, Sept. 21, 1912).

Laguesse and Opie have put forth the supposition that this secretion is derived exclusively from the islets of Langerhans. But the cells of the pancreatic acini and those of the islets are of identical origin and of like nature. It appears very probable, therefore, that the first-named may yield some principle to the lymphatic or blood- capillaries. This view represents more than a hypothesis. Personal researches have, indeed, shown that the primary effect of ligation of the duct of Wirsung is to augment greatly the glycolytic power of the blood. Now, the islets of Langerhans are not in communication with the excretory ducts, and an excessive pressure in the latter can react only upon the cells of the acini.

A most conscientious Danish anatomist, Heiberg, lays great stress upon the decrease in the *number* of the islets in certain cases of diabetes. This observation is of much interest, but is not possessed of the meaning which one might well be tempted to attribute to it; it does not prove that the islets are exclusively internally secreting structures. To my thinking, it can be explained as the result of diminished activity of the pancreatic parenchyma, which has become incapable of forming new islets.

The most recent and reliable investigations all confirm the view that the islets of Langerhans are not the exclusive source of the internal secretion of the pancreas. This is also the conclusion reached by U. Lombroso after a thorough discussion of the pathological data (Ergebn. der Physiol., 1910, ix, pp. 43-47), and that of Wynen (Arch. des sci. biol. de St. Petersb.) and of Hansemann (Berlin. klin. Woch., 1912, No. 20).

The function of the pancreatic internal secretion is not limited to the favoring of glycolysis; it is also generally accepted that it is operative in the *fixation* of carbohydrates (Chauveau and Kaufmann, Pavy). It may perhaps be of use in other ways. U. Lombroso believes that it contributes to the absorption of fats.

> In 9 out of 18 cases of arteriosclerotic changes in the pancreas studied *post mortem* by the writer, glycosuria was evident in 9. The arteriosclerotic lesions were much more pronounced in the cases accompanied by glycosuria. The islands of Langerhans were always affected in the latter, and proportionately to the intensity of the diabetes. The lesions in the diabetic subjects always predominated in the tail of the pancreas. Hoppe-Seyler (Deut. Archiv f. klin. Med., Bd. lxxxi, Nu. 1-2, 1904).

The writer in 200 pancreases removed from cadavers, found degenerated, inflammatory, circulatory, and neoformative changes. The four cases of diabetes showed, in keeping with the views of Hansemann, Lawrence, and others, atrophic changes throughout this organ. His findings did not agree, however, with those of Opie, Massari, and others, who claimed that the characteristic changes in the pancreas of diabetics were found in the islands of Langerhans. He admits having found the changes in the latter described by these authors, but he also found the same changes in various other diseases. Moreover, he was able to find frequently that the entire gland was atrophied and believes that the lesions of the islands are simply part of the general lesion of the entire organ. Ghedini (Riforma Médica, Aug. 3, 1904).

In 11 cases of diabetes the entire parenchyma of the pancreas was more or less degenerated, but the islands of Langerhans, for the most part, were normal. In some instances they had evidently proliferated. This proliferation and the general aspect of the islands suggested vicarious action on their part and regeneration of the acini from these islands. Karakascheff (Deut. Archiv f. klin. Med., Bd. lxxxii, Nu. 1-2, 1905).

The writer examined the pancreas in 36 cases of diabetes. He regards changes in the parenchyma of the pancreas as the cause of diabetes rather than selectively in the islands of Langerhans. Recent researches by Karakascheff and Reitmann has converted them also to this opinion. In 5 cases described in detail, the alterations in the parenchyma of the pancreas were very pronounced. They were accompanied also by the efforts at regeneration characteristic of cirrhosis of the pancreas. Herxheimer (Virchow's Archiv, Bd. clxxxiii, Nu. 1, 1906).

Autopsy records of 90 cases of diabetes, special attention being paid to the lesions in the pancreas. There were found:—

(*a*) Lesions of the parenchyma and interstitial tissue proper, and

(*b*) Lesions of the islands of Langerhans.

The tabulated result of his case analyses is as follows:—

(1) *Chronic inflammation of the pancreas.*

	CASES.
Interacinar pancreatitis; sclerosis of the islands of Langerhans	39
Interlobular pancreatitis; sclerosis of the islands of Langerhans	4
Interacinar pancreatitis; hyaline degeneration of the islands of Langerhans	19
Interacinar pancreatitis with lipomatosis; sclerosis of the islands of Langerhans	2
Interacinar pancreatitis with siderosis of the islands of Langerhans (hemochromatosis)	2
(2) *Parenchyma normal; lesions of the islands of Langerhans.*	
Sclerosis of the islands of Langerhans	4
Hyaline degeneration of the islands of Langerhans	7
Infiltration of leukocytes about the islands of Langerhans	1
(3) *Pancreas normal*	11
	90

Of the 11 cases with a normal pancreas 5 showed marked diminution in the number of islands of Langerhans. In 5 other cases the pancreas was abnormally small.

These lesions are not secondary to diabetes, but are primary, as shown by the variety of lesions found. The essential cause of pancreatic diabetes is shown to be a lesion of the islands of Langerhans because, as the case analyses show, lesions of the islands with normal parenchyma often occur, while many cases of interlobular pancreatitis without lesions of the islands occur in cases of duct obstruction without any signs of diabetes having been present during life. Cecil (Jour. of Exper. Med., March 1, 1909).

Although it is now nine years since Opie first described the occurrence of definite lesions in the islands of Langerhans in diabetes, we are still uncertain as to just what relation these structures and their pathologic alterations may have to diabetes. While there are those who have gone as far as Dale and denied the very existence of the Langerhans islands as independent structures, and others have disputed their relation to carbohydrate metabolism, the balance of evidence and the weight of opinion are now altogether in favor of considering them as specific organs of internal secretion which are concerned in carbohydrate metabolism. Just what part they play in this process, or how they do it, are admitted to be unsettled problems. The occurrence in Cecil's report of so many cases in which the changes in the pancreas are but slight or entirely absent leaves open the question as to whether the pancreatic lesions may not be the result rather than the cause of the diabetes. In the cases in which no pancreatic lesions are present, it must be admitted that here, at least, the diabetes is not of pancreatic origin, and presumably the same is true in many of the cases in which pancreatic lesions are present but of slight degree.

In view of the essential importance of the liver in sugar metabolism the hepatic changes of diabetes would seem to be fully as significant as the pancreatic lesions, and worthy of the same careful study. It may be that a comparative study of the changes in these two organs, correlatd with the clinical and chemical manifestations of selected cases, will be able to throw new light in some of the obscure places. Editorial (Jour. Amer. Med. Assoc., May 15, 1909).

The writer found glycosuria mentioned in only 3 of 35 cases of pancreatic cancer whose records he had examined, and it was never very pronounced. In a case he reports in detail the diabetes was most probably primary, the same as in a case reported by Lépine in 1909. In both these cases the diabetes had existed for eighteen months and several years and the cancer was of comparatively recent development. Heiberg (Deut. Archiv f. klin. Med., Bd. cii, Nu. 5-6, 1911).

The writer found the islands of Langerhans strikingly pathologic in the 183 cadavers of diabetics examined while no changes of the kind in the islands could be detected in the 73 cases of chronic tuberculosis also examined *post mortem.* The findings demonstrated that it is not any special changes in the islands but the extent of involvement which determines the development of diabetes. In some non-diabetics the parenchyma was found atrophied while the islands were not much degenerated. A. Weichselbaum (Wiener klin. Woch., Feb. 2, 1911).

The problem has been confused by accusing the islets of Langerhans, which as the supposed source of the internal secretion of the pancreas would naturally be found affected in diabetes. It has now been demonstrated that the latter affection may exist with intact islets, while in destruction of the latter it may be absent. The opinion has gained ground that the islets are in no wise distinct in nature from the ordinary parenchyma, and it is known that the latter is the source of the former. The pancreas is always the seat of structural changes in diabetes, which latter is necessarily due to derangement of the harmonic functions of that gland. Van Hansemann (Berl. klin. Woch., May 13, 1912).

Other Internal Secretions.—The internal secretion of the thyroid gland and especially that of the adrenals tends to increase the amount of sugar in the blood. It would even appear that the latter is indispensable for the production of a hyperglycemia.

[See on this point Dr. Sajous's work on the "Internal Secretions," Vols. I and II. The reader will find therein a discussion of all the details of the subject, which cannot be given here. In Sajous's opinion, advanced in the above volumes (1903-1907), both the adrenals and thyroid, when overactive, can produce diabetes by increasing, through their secretion, abnormal oxidation and metabolism in the pancreas. The latter organ being thus caused to produce an excess of amylopsin which in turn acts on the hepatic glycogen, sugar is formed beyond the needs of the tissues at large, and the surplus of sugar is eliminated with the urine. This he terms the *sthenic* form of diabetes mellitus. In what he terms the *asthenic* form, the adrenals and thyroid are insufficient and metabolism in the pancreas being correspondingly impaired, alimentary glycosuria occurs precisely as it does after removal of the pancreas or to a less degree when disease of the pancreas inhibits its functional activity. R. LÉPINE.]

The views at present held with regard to the interaction of the ductless glands and their part in the production of diabetes are to some extent theoretical, and this is particularly so as regards the chromaffin system, but they correlate in a much more satisfactory manner than has previously been possible the experimental data that have accumulated as to the effects of these organs on carbohydrate metabolism, and they bring into line the known facts in the etiology of diabetes. Whether subsequent observation confirms, or in part disproves, these theories, there can be no doubt that they open up a wider conception of the possible pathology of glycosuria, and indicate that it is not a sign of one disease, but a symptom common to several diseases. P. J. Cammidge (Pract., Feb., 1912).

The essential and primary disturbance may be in one or another of the ductless glands. A marked correlation of the internal secretions of the ductless glands is beyond question. The internal secretions of the adrenals (chromaffin system) and pancreas mutually retard action. An important function of the adrenals is to set free the carbohydrates in the liver, and possibly in other storehouses also. Normally this influence is exactly balanced or counteracted by the hormone contained in the pancreatic internal secretion, resulting in a normal flow of sugar from the liver. If the chromaffin system is overstimulated, as it may be through the sympathetic nervous system, there is an overproduction of the "accelerator" hormone of the adrenals, and the "retarding" hormone of the internal secretion of the pancreas is overbalanced, the glycogen in the liver is rapidly set free, and a hyperglycemia and glycosuria result. Pancreatic diabetes is produced in a similar manner. The glycosurias in pituitary and thyroid diseases may be explained in a somewhat analogous manner. There are fewer adherents at present to the theory that hyperglycemia results from deficient consumption or oxidation of glucose in the tissues. T. B. Futcher (Jour. Amer. Med. Assoc., Dec. 21, 1912).

Injections of epinephrin made when the pancreatic secretory flow, following removal of the adrenals, is at its height, inhibit the flow. Shortly after or before the blood-pressure falls to its previous level, the pancreatic flow returns. It can thus be repeatedly inhibited and it then repeatedly returns. The tendency to flow seems very strong. Since removing the adrenals induces a flow and since injections of epinephrin then inhibit the flow; and since the flow returns when the effect of the injection wears off (which last can be repeatedly demonstrated in one animal), it is difficult to escape the thought that there is normally some such relation between these glands. Pemberton and Sweet (Archives of Internal Med., Sept. 15, 1912).

The secretion of the hypophysis appears to be operative in the same direction. While glycosuria and even true diabetes may follow Basedow's disease, cases of diabetes dependent upon a tumor of the hypophysis, generally but not always with concomitant acromegaly, are known to occur.

[One of the first cases published was that of an acromegalic woman in my service. The urine contained 70 grains of sugar per liter. (See my book "Le Diabète sucré," Paris, 1909, p. 439; A. Delille: Thèse de Paris, 1908. For cases without acromegaly, see Lucien and Parisot: Rev. neurol., 1909, p. 970. R. LÉPINE.]

It is quite certain that disorders of the other internal secretions may favor the development of diabetes. (Apert: Nouv. icon. de la Salpêt., 1904, and Spillmann, Jeandelize, and

Parisot: Soc. de Biol., 1910, Mar. 19, have reported cases of diabetes which appeared to depend upon a condition of infantilism.) These secretions are subject to influences of the nervous system, and it is not impossible that diabetes is, in a certain number of cases, dependent upon an excitation of the sympathetic, the influence of which exceeds that of the antagonistic nerves (the autonomous nerves of Langley). (See Eppinger, Falta, and Rudinger: Zeitschr. f. klin. Med., 1908.)

Formerly it was assumed that the glycosuria resulting from puncture of the medulla ("sugar puncture") was due to direct stimulation of the liver from the central nervous system, but recent research has demonstrated that this stimulation is transmitted by the left sympathetic nerve and at first to the left suprarenal, whence the stimulation is forwarded to the right suprarenal by the connecting nerves. If the left suprarenal is cut off from the left sympathetic nerve, no glycosuria follows the sugar puncture. Puncture of the medulla stimulates the suprarenals to greater secretion, and this secretion in turn stimulates the liver to an excessive output of sugar. A number of toxic influences act in the same way, partly by the influence on the sugar center in the medulla, partly by stimulation of the sympathetic nerve or the suprarenals, thus causing exaggerated functioning which entails overproduction of sugar in the liver. These facts explain the influence of the central nervous system on the intensity of diabetic glycosuria and show the necessity for studying each individual case with special care, and the importance of warding off emotional stress and injurious nervous and toxic influences. C. von Noorden (Med. Klinik, Jan. 1, 1911).

PATHOGENESIS. — Hyperglycemia, the proximate cause of diabetes mellitus, is itself the result of a diminution of the glycolytic power of the tissues, to which is superadded very often a certain state of *lability* of the carbohydrates of the organism.

Diminution of Glycolysis.—Twenty years ago I showed, with Barral, that glycolysis is lessened in the blood of diabetics, and that their tissues consume less sugar than is the case in the normal state. (See Rev. de méd., 1910, p. 424; the decrease of glycolysis in the blood of diabetic dogs was fully confirmed by Vandeput in the laboratories of Prof. Slosse, of Liége, in January, 1910.) It is not a fact that oxidation is lessened in them; Nencki and Sieber proved a long time since that the oxidative processes are as active as in normal subjects. The true condition is that the tissues of diabetics are incapable of splitting the glucose molecule as well as in the normal state. In the healthy animal, this process of cleavage, which is the essential factor in glycolysis, is favored by the internal secretion of the pancreas, which operates very effectively as a species of sensitizing substance (De Meyer).

[To Cohnheim is sometimes attributed the idea that the pancreas acts *by favoring* general glycolysis. That is not the fact: I expressed this opinion in very explicit terms five years before Cohnheim ("Le Diabète et son traitement," Paris, 1899, p. 26), and it was De Meyer who developed the idea to a more precise conclusion. R. Lépine.]

Lability of the Carbohydrates.—Diminution of glycolysis to a greater or less extent exists in all diabetics. Furthermore, in the majority of them at least, a rather complex condition is observed, which may be roughly termed lability of the carbohydrates and which consists in a more ready transformation of glycogen into sugar, as well as in the fact that the protein molecule gives off sugar more easily than under normal conditions. Another peculiarity in this lability of the sugar is that the virtual sugar of the blood passes very easily into the state of free sugar. Thus, when a dog is thoroughly bled, the virtual sugar in its blood will cease to be combined, *i.e.*, to fail to react with the reagents for sugar. It will become free, whence the more or less marked hyperglycemia observed after extensive bleedings. (See Lépine and Boulud: Soc. de Biol., 1910, and Jour. de physiol., March, 1911.)

What is the explanation of the more active formation of sugar in diabetes? For some time I have been putting forth the idea that we have to deal, in this connection, with one of those reactive processes so common in the organism, and in which, as in many defensive reactions, the mark sought is overshot: the system is suffering from the deficient combustion of glucose; through a blindly executed reactive process, it forms still more of it, as, for example, a man devoid of intelligence, feeling cold and not noticing the fact that his stove was not drawing well, might fill it completely full with fuel.

The Numerous Varieties of Diabetes Mellitus.—The deficiency in the cleavage of glucose in diabetes may be more or less pronounced. There are also infinite variations in the lability of the carbohydrates. These are the causes which lead to the multiplicity of varieties of the disease. It is not because one diabetic has a pancreatic lesion, another a lesion of the nervous system, while a third has no lesion that is appreciable, that these three diabetics differ the one from the others; it is merely because the modalities of glycolysis, of glycogenesis, etc., are different. It is physiological and clinical analysis, and not pathological investigation, which permits of the establishment of separate varieties of diabetes.

The Blood in Diabetes.—Hyperglycemia, the result of deficient glycolysis and often of excessive glycogenesis, is the essential morbid phenomenon in diabetes. The quantity of sugar contained in the blood varies in general from 2.5 to 5 Gm. of sugar in each 1000 Gm., rarely less and rarely more.

Diabetic blood decolorizes a certain number of coloring substances, *e.g.*, methylene blue, if it is added to the latter in the ratio of 20 mg. of blood to 1 c.c. of a 1:6000 solution of the coloring agent. This is **Williamson's test.**

Bremer's reaction is exhibited in the greenish coloration assumed by dry red corpuscles, fixed upon a glass slide, when they are treated with a mixture of eosin and methylene blue. Red corpuscles from normal blood under the same conditions assume a pink color. I had occasion to observe with Lyonnet—and Bremer admitted it—that this reaction is not peculiar to diabetic blood. We obtained it also with red corpuscles from leukemic blood. The reaction is, therefore, of but limited value.

The Renal Element in Diabetes.—Blood under normal conditions contains about 1 Gm. of sugar to the liter. Normal urine, on the other hand, contains only a few cg. of it in the same amount. It is quite certain, moreover, that the glycosuria in diabetes mellitus does not bear a strict relationship to the hyperglycemia. In a short time after removal of the pancreas—*e.g.*, at the end of eight to ten hours—the hyperglycemia hardly exceeds 2 Gm., and yet the glycosuria is already very pronounced; on the contrary, thirty or forty hours later, *i.e.*, forty and odd hours after the pancreatectomy, with the animal in starvation, the hyperglycemia is very marked, while, because of the inanition, the glycosuria is but slight. Again there are reasons for believing that the discrepancy in this respect, sometimes pronounced, is in part owing to the intervention of a renal factor (Lépine: Sem. méd., 1895, p. 383).

A number of years ago, I reported the rather extraordinary case of a woman the subject of both Bright's disease and diabetes whose blood, on the last day of her existence, contained about 10 Gm. of sugar to the liter, and in whom glycosuria was nevertheless exceedingly slight (Rev. de méd., 1897, p. 832). The assertion is consequently warranted that, where the permeability of the kidneys is greatly reduced, the glycosuria is but slight in comparison with the degree of hyperglycemia.

> Case of a man, aged 45 years, who had constant polyuria for fourteen years. Alcoholic excesses caused transient albuminuria; during the last six years there has been also transient glycosuria with hyperglycemia. After a few weeks of rest and dieting both sugar and albumin disappeared from the urine. With care the man may escape serious trouble. G. Roque and J. Chalier (Arch. des Mal. de l'App. Digestif, Dec., 1913).

SYMPTOMS.—With but rare exceptions, the onset of this disease is insidious, and cannot be recognized by the patient. Many cases of diabetes remain entirely unsuspected until the time when some symptom other than the glycosuria attracts the attention of the patient. This may be either excessive thirst, polyuria, unusual weakness, or even impotence. More rarely, it is a sudden diminution of the acuity of the vision, or perhaps a complication in the form of furunculosis or balanitis in men, and pruritus vulvæ in women. The daily quantity of urine is increased, except in some rare cases, classed under the head of *"diabetes decipiens."*

> Initial symptoms of diabetes mellitus in children are apt to be incontinence of urine, nervous irritability, and great thirst. Strength, flesh, and color may sometimes be retained until nearly the end. A gain of weight and height, even, may occur, without any amelioration of the disease. Townsend (Boston Med. and Surg. Jour., May 11, 1899).

Urinary Symptoms.—The urine is pale in color; the reaction is sometimes unmistakably acid; the specific gravity, except in some very rare cases, is very perceptibly increased (1025 to 1045 and even 1050 has been met with). The odor is sweet, owing to the presence of glucose, which may amount to, or even exceed, 8 per cent. Generally speaking, the quantity indicated by Fehling's test is a little greater than that registered by the polarimeter. This is due, first, to the fact that the urine contains reducing substances which do not deviate the plane of polarized light, and, second, to the fact that in a number of cases of severe diabetes beta-oxybutyric acid salts are present in the urine, which deviate it to the left in such a manner that a portion of the deviation to the right, due to the glucose, is masked.

In mild cases of diabetes the true beta-oxybutyric acid is not present in the urine; there may, however, be other substances which deviate polarized light to the left, especially levulose, which has very rarely been met with in diabetes, to the exclusion of the glucose (Zimmer, Külz, Seegen, Neubauer).

> Three cases of levulosuria in diabetes. In one of the writer's cases the excretion of levulose was urinogenous, *i.e.*, dextrose was inverted to levulose in the bladder, or after being passed, owing to the alkaline reaction of the urine. There was no alimentary levulosuria. The fact that alkaline solutions will invert glucose has long been known to chemists and explains some of the cases of levulosuria in the literature. In the second case the levulosuria ceased on stopping the administration of an alkaline mineral water, though the urine was acid; here the author believes that dextrose was inverted in the alimentary canal by the action of the alkali and supports this by the following experiment: After 100 Gm. (3⅓ ounces) dextrose, no levulose appeared in the urine, but when alkaline water was given with the dextrose, levulose was excreted. Koenigsfeld (Zeit. f. klin. Med., Bd. lxix, Hft. 3-4, 1909).

Other sugars have sometimes been found; for instance, traces of pentose (Salkowski, Külz), inosite, etc. Külz and Vogel found a mixture of dextrosazone and pentosazone in the urine of 76 out of 80 cases of diabetes. In 64, reaction positive; in remaining 12 cases, doubtful. Pentoses occur, however, in but minute proportion compared to glucose.

Albuminuria exists in diabetes in at least one-third of the cases, but in only a few cases is it symptomatic of Bright's disease.

Urea.—Owing to the polyuria, urea is naturally only present in the urine in a very small proportion, but the daily quantity of this substance is often increased. In this respect one may distinguish two classes of diabetics, according to whether the urea is normal or augmented in relation to the patient's body weight. An excessive catabolism of nitrogenous materials is an important morbid factor in diabetes. The relation of urea to the total nitrogen is not noticeably altered, except in grave cases of diabetes, in which the proportion of ammoniacal salts is, as is well known, greatly increased, in order to overcome the acid dyscrasia.

Uric Acid.—Very contradictory assertions have been made concerning the excretion of uric acid in diabetics. In reality the *exogenous* uric acid is naturally abundant in those eating a great deal of meat. As for the *endogenous* uric acid, it is a rare occurrence for it to be increased in diabetics; in fact, as a rule it is diminished. In severe cases of the disease an abnormally large amount of the alloxuric bases has at times been detected. This product is often considerably increased, in most instances owing to the meat diet, and, though very infrequently, as a result of the denutrition incident upon the disease.

Ammonia.—The increase in the urinary ammonium in a few diabetics was pointed out by Boussingault in the first half of the last century. Its significance was recognized later, when it became known that the production of ammonia in the diabetic subject is often a defensive measure on the part of the economy against acidosis.

Lactic and Oxalic Acids.—These acids are sometimes present in excess in diabetic urine, and a few cases have been reported in which the proportion of oxalic acid present was enormous. These are, however, exceptional disturbances of nutrition, constituting in reality a complication of diabetes.

Chlorides.—The proportion of chlorides in the urine generally does not present any marked change; there are, however, cases in which a distinct choluria is present (Ascanio Rodriguez).

Calcium.—The excretion of calcium salts is considerably increased in the severe forms of diabetes, while in mild forms it is the same or only slightly in excess of that met with in healthy persons.

Iron.—An increase in the excretion of iron, probably in relation with augmented hemolysis, has at times been noted.

Cardiovascular Symptoms. — Hypertension is rather frequently present in diabetics. A certain proportion of the cases show arteriosclerosis and sometimes present signs of cardiac weakness, viz., a tendency to embryocardia, a considerable degree of acceleration of the pulse when the patient changes from the recumbent to the vertical posture, etc. Such a condition of the circulatory system is truly a complication of the disease, and as such must be taken into account in the prognosis of diabetes.

> Results of blood-pressure observations in 25 cases of diabetes, 13 males and 12 females, 13 of them under 50 and 12 of them over that age. The average blood-pressure of the former was 107 mm., and of the latter 150 mm. Their average weight was 138 for those under 50 years and 175 for those over that age. Age and weight are thus apparently of importance in determining the degree of blood-pressure. Acid intoxication (diceturia) was observed in 9 of the 13 cases under 50, and in only one of the others. The degree of glycosuria had no apparent effect on the blood-pressure; in 15 of the 20 there was a maximum glycosuria of over 3 per cent., and the average blood-pressure in these was 121 mm. In the other 10 cases it averaged 135 mm. So far as a conclusion can be drawn from these cases, it is that an inverse ratio exists between the degree of glycosuria and the blood-pressure. This might be looked for, as the milder cases of diabetes are apt to be in elderly persons with some arteriosclerosis and consequent high pressure. As regards acid intoxication, it would seem to be attended with hypotension, owing probably to the generally more asthenic conditions in these patients rather than to acid toxins acting directly. In no case was the excessive hypertension declared by Potain and Teissier to be characteristic of diabetes observed. All the evidence points to the fact that it is to the complications, especially arteriosclerosis and chronic nephritis, that we must look for the cause of the cardiovascular secondary conditions. A. R. Elliott (Jour. Amer. Med. Assoc., July 6, 1907).

Contrary to what one might have supposed, the heart is found of small size and the myocardium pale at autopsy in almost one-half of diabetic cases. In one-third, however, I have found the heart enlarged. The hypertrophy of the organ is sometimes dependent upon renal sclerosis or generalized arteriosclerosis; at other times, in relation with a (primary) increase in size of the other organs. As a matter of fact, diabetes does not spare arthritics of massive build and possessing large organs originally than it does other individuals.

Digestive Functions.—It will easily be realized that the ingestion of an excessive amount of liquids and solids must sometimes lead to disturbances of the gastric digestive function. These disorders seem to depend oftener upon achlorhydria than upon hyperchlorhydria.

In view of the frequency of pancreatic lesions in diabetics, one might suppose *a priori* that the utilization of foodstuffs would often be imperfect in them. But this supposition is not confirmed by the observed facts: the balance of ingested nitrogen and nitrogen excreted in the urine shows that in all but exceptional cases the deficit is slight. Fats, it is true, may not be utilized altogether as well as protein materials. As for the digestion of starchy substances, it is perfectly well carried out.

Symptoms Relating to Respiratory Apparatus.—Diabetics who do not suffer from pulmonary complications show no morbid phenomena in this direction except an increase in the gaseous interchanges in grave cases and a lowering of the respiratory quotient, due, in turn, to the deficient destruction of glucose.

> Dyspnea, when urgent, is always a grave sign in diabetes. When it develops, one must examine the chest very closely for evidence of tuberculosis or other pulmonary trouble, and also the urine for evidence of acetone or diacetic acid, remembering that this may be present even when, or particularly when, the sugar has shown signs of diminishing. When the sugar diminishes and dyspnea is worse, it is almost always certain that acetone or oxybutyric acid of diacetic acid will be present. When air hunger develops in patients who are not known to be diabetic, or who are known not to be diabetic, or when there is marked apathy or drowsiness in patients who are being fed by the rectum, it is advisable to examine for acetone and diacetic acid, and when these substances are present, whether one is dealing with diabetes or not, it is always a safe rule to give alkalies and carbohydrates. N. Tirard (Clinical Journal, April 5, 1911).

General Nutrition.—The diminution of glycolysis in diabetics is subject to wide individual variations. In a few, it is but slight. It is to be borne in mind, too, that certain sugars are more perfectly utilized than glucose. The latter is, however, always utilized at least in part. When insufficiency of glycolysis in diabetes is referred to, the implication is that the process is more or less reduced, but not completely abolished.

Still more varied are the modalities relating to glycogenesis and to what I have termed the lability of sugar. All sorts of combinations of the several factors may present themselves, with the result of rendering diabetes, among the diseases of nutrition, the most complex in its pathogenesis and the most protean in its symptomatology.

It would seem at first sight inevitable that an increased catabolism of the proteins (and of the fats) should take place in order to compensate for the lack of calories resulting from the faulty utilization of the carbohydrates. Yet, while in certain diabetics the destruction of protein materials exceeds the normal by more than 30 per cent., in others it remains within ordinary limits. I have seen a patient of normal body weight, with inherited diabetes, who remained without glycosuria as long as he limited his ingesta to 2 liters of milk, but developed glycosuria when a slice of meat was added to the milk; this was a diabetic with slowed nutritional processes who was unable to stand a normal food ration.

It is not certain, indeed, whether the increased breakdown of proteins, in cases where it occurs, represents a response to an actual need on the part of the organism. It may in part be the result of a bad habit. This would seem to be proven by the fact that if the ingestion of meat is restricted the urea excretion gradually returns to the normal. Among other unfavorable effects, the excess of proteins causes an increase in the glycosuria. There are, however, exceptions to this —indeed, exceptions to rules are without number in the pathology of diabetes: Naunyn has seen a diabetic 28 years old who remained without glycosuria upon a diet consisting exclusively of 1500 Gm. of meat per diem,—a very unusual circumstance, since glycosuria is almost always increased when meat is taken to excess.

The degree of glycosuria may, indeed, be asserted to vary according to the nature of the proteins ingested. In general, meat and casein increase it. Fats do not appear, in the vast majority of diabetics, to cause an increase. They tend rather, if not to initiate, at least to augment acetonemia.

COMPLICATIONS. — The complications of diabetes are numerous. It is necessary to distinguish those which are accidents superimposed upon the disease, *e.g.,* phlegmonous processes which are the result of infection, from those complications which form part, as it were, of the diabetic process. Among the latter, acetonemia must be placed in the front rank, and will be discussed first.

Acetonemia, or Acidosis.—The healthy average individual eliminates daily about 20 mg. of acetone through the respiratory tract; a trace of it is also excreted in the urine. If the subject is starved for two or three days, much more acetone will be eliminated. In addition, he will excrete diacetic acid, as shown by means of Gerhardt's test, and even oxybutyric acid. This process of elimination of the acetone bodies occurs owing to the fact that the system is deprived of carbohydrates. Now, in severe diabetes, *with markedly diminished glycolysis,* the system is in reality likewise deprived of carbohydrates, for the reason that the glucose present in the blood and tissues *cannot be utilized.* Diabetic acetonemia is thus, in a sense, the necessary result of every diabetes accompanied by a marked decrease of glycolysis. Furthermore, when a diabetic is subjected to a carbohydrate-free diet he is being exposed to the more or less early production of acetonemia.

The source of the acetonemic substances is in the proteins and in the fats. This has been shown by recent investigations, among which should be mentioned those of Embden, of Dakin (Jour. of Biol. Chem., vol. iv *et seq.*), etc. But notwithstanding numerous researches, we are still in ignorance concerning the process by virtue of which many grams of acetone bodies can be produced daily by the organism.

The acetonemic dyscrasia has also been designated as *acidosis,* an expression *en partie* justified by the fact that acetonemia consists essentially of an accumulation in the system of organic acids — diacetic and beta-oxybutyric acids. It is to be remembered, however, that this form of acidosis is different from that induced by injecting into an animal a solution of a mineral acid. It is a *special* form, as I have shown (Rev. de méd., 1887), calling attention to the fact that blood containing acetone bodies is more toxic than it would be did it contain an equivalent of an inorganic acid.

The experimental investigations of the writer sustained the assumption that acidosis is the main factor in diabetic coma. None of the mineral acids induced any tendency to coma in the animals, but the organic acids, such as butyric, lactic, propionic, and beta-butyric acids all had marked though variable power to induce coma. The acids free from a secondary alcoholic action, such as butyric and propionic acids, displayed the most powerful coma-producing action. The research confirms the importance of alkaline treatment of diabetic coma and in prophylaxis. Labbé and Violle (Presse méd., April 8, 1911).

Moreover, it is very probable that in the condition we term "acetonemia" acetone bodies are not the only toxic substances (See below: ACETONEMIC COMA.)

That diacetic acid and acetone are derived from beta-oxybutyric acid is a generally accepted fact. But the opposite process may also occur, and diacetic acid yield, by synthesis, oxybutyric acid.

Acetonemia, which occurs with great frequency in severe cases of diabetes, brings on numerous morbid results, of which the most serious is coma. This will be considered later. (See also the article on ACETONURIA, for tests, etc., in the first volume of the present work.)

It also gives rise to *lipemia,* a less common condition which is the result of decomposition of the lipoids in the system, probably because of a lack of alkalinity. In these cases the blood contains a large amount of fat,—as much as 100 Gm. in 1 liter of blood. The blood presents the appearance of chocolate to which milk has been added. This fat consists to a large extent of olein; but lipoids, lecithin, and especially cholesterin are also present in large proportions. The condition is thus in reality not only a lipemia, but a *lipoidemia.*

Of the three acetone bodies, beta-oxybutyric acid, diacetic acid, and acetone, the first named seems at present to be the cause of acidosis, not on account, however, of any specific toxic properties, but simply on account of its excess robbing the body of its alkaline supply. Any other acid present in similar excess might have the same result. Fat, especially that containing fatty acids, is the principal source of the acetone bodies, though they may be derived from protein. The place of formation is probaly the liver. Goodman (Archives of Intern. Med., May, 1908).

Having thus taken a general view of acetonemia, which is, on the whole, the result of a deficient combustion of the carbohydrates, let us consider the other complications of diabetes.

Nervous System.—The most common secondary nervous lesions of diabetes are certain peripheral neuroses, especially those which result in the abolition of the knee-jerk. Condition of the knee-jerk was tested by Grube in 184 cases of diabetes mellitus. As only 1 examination was made in 56 of the cases, these are excluded from consideration. Of the 128 remaining cases, the knee-jerk was normal in 113 and increased in 2. In the latter cases the patients were suffering from a severe form of diabetes. In 4 cases of severe diabetes the knee-jerk was absent or greatly diminished. The phenomenon was absent in 9 slight cases. Excluding 3 of these,—because 2 of the patients were tabetic and the third was too obese to admit of satisfactory examination,—there were only 10 patients (7.6 per cent.) in whom the knee-jerk was abolished or much reduced.

R. T. Williamson, in an analysis of 50 cases, found both knee-jerks absent in 50 per cent., both present in 38 per cent., and feeble or absent on one side in 12 per cent. In patients under 25 years the knee-jerks were absent in 80 per cent.; under 30 years, absent in 75 per cent.; over 30 years, absent in 46 per cent.

The other nervous symptoms are pain and, more rarely, paralysis. It has been known for a long time that the neuralgia of diabetes is very painful and difficult to cure. Worms has noted that it is very often symmetrical, and states that the pain increases and decreases with the hyperglycemia, which is certainly inconstant. Ziemssen was the first to refer this neuralgia to a neuritis. There are also shooting pains that somewhat resemble those of ataxia, and which may, in some cases, suggest the question as to whether there is not actual tabes: a very difficult problem to decide.

Vergely reported a case in which there were pains resembling those of *angina pectoris.*

[In a case of diabetes witnessed by Sajous the paroxysms of angina pectoris were very severe; the attacks yielded readily to inhalations of amyl nitrite. They failed to recur after alkaline treatment and an increase of carbohydrates had caused acetone and diacetic acid to disappear from the urine.]

> Attacks of pain, even simulating "gastric crises," are sometimes forerunners of diabetic coma. In two cases witnessed by the writer, the question of a possible grave abdominal emergency being imminent arose. In each case, however, the presence of dyspnea, together with the fact that the patients were known to be diabetic, suggested the imminence of diabetic coma, and in each case coma did, in fact, ensue with rapidly fatal results. The pain may be due to some toxic affection of the solar plexus, and points out the importance of recognizing it so that early and adequate alkaline treatment may be instituted. Lereboullet (Progrès méd., Dec., 1911).

Of the possible *trophic disturbances,* perforating ulcer is the most serious.

The *paralyses* of diabetes present themselves as follows: 1. Limited and incomplete paralysis; this is, by far, the most prevalent form, as has been stated by Bernard and Féré. 2. Monoplegia. 3. Hemiplegia. 4. Paraplegia. The various forms of diabetic paralysis are sometimes associated, or are combined, with certain unusual phenomena, *e.g.,* facial hemiplegia preceded by facial neuralgia and falling of the upper eyelid (Charcot, quoted by Bernard and Féré), or paresis of the extensors of the left thigh, impeded speech and deviation of the mouth to the left (Charcot, *ibid.*), etc. The progress of these paralyses is also somewhat peculiar: they are sometimes migratory and transitory. Some of them are undoubtedly of central origin, but the majority are of peripheral origin, a neuritis forming their anatomical substratum. The peripheral variety is not exempt from this rule, as is proved by the existence, in diabetic paraplegia, of the symptom-complex to which Charcot has given the name *steppage,* which is characterized by the lowering of the forward part of the foot in walking. This we know is due to paralysis of the extensors of the foot, and it occurs in peripheral neuritis, but not in myelitis.

Cramps are another motor disturbance met with in diabetic subjects. These occur principally in the lower extremities, and at night they occasion *insomnia,* which, according to

Bernard and Féré, appears to be, in diabetic subjects, the first symptom of disturbance of the cerebral circulation, and may sometimes prove the forerunner of serious symptoms.

Convulsions are rare. I have met with a few cases in which they occurred, but, as the autopsies showed, they were not due directly to the diabetic hyperglycemia, their immediate cause being lesions in the motor areas of the cerebral cortex, brought on through the influence of the diabetic dyscrasia.

> Although some of the epileptiform attacks which occur in the course of diabetes are manifestly due to other associated conditions (uremia, cerebral softening, meningitis, etc.), a certain proportion of them are unquestionably related directly to the diabetes itself and are the expression of some form of diabetic intoxication. Such attacks may simulate closely the general convulsions of true epilepsy, or they may be distinctly Jacksonian in character and be limited to one side of the body or to certain groups of muscles. These localized convulsions are usually associated with transient paralysis of the affected muscles, aphasia, sensory disturbances, or other symptoms suggestive of a circumscribed brain lesion, and may thus lead to serious errors in diagnosis.
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> The convulsions may apear only during the terminal coma, or they may be repeated at frequent intervals for days or weeks before coma develops, or, finally, they may cease with improvement of the diabetic symptoms.
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> The association of such epileptiform attacks with the signs of acid intoxication is by no means constant. In several of the cases it is certain that no such acidosis existed. It seems probable, therefore, that the cause of the convulsive attacks must be sought for in some other form of diabetic intoxication. L. A. Conner (Med. Rec., May 16, 1908).

Narcolepsy and Mental Disturbances.—More frequently narcolepsy, *i.e.*, a condition of irresistible tendency to sleep, has been noted in obese diabetics. The obesity is the principal cause of this trouble. As for the mental disturbances, they have been carefully studied by Legrand du Saulle. Generally they are characterized especially by melancholia and, in particular, by the fear of being ruined. The chronic vascular lesions in the brain constitute their chief cause; but it also seems certain that the diabetic dyscrasia itself plays a rôle in their production, as they are often observed to disappear or at least to improve when the hyperglycemia and acetonemia are reduced.

Coma.—Coma is by far the most serious of the nervous complications of diabetes; its termination is almost always in death.

1. *Cardiac coma:* In a few cases, relatively quite rare, the findings at autopsy are limited to lesions of the heart. Frerichs has drawn attention to these cases, and I have reported a typical example: The patient, who was somnolent when brought to the clinic, showed not a trace of acetonuria, and was relieved exclusively by digitalis.

2. *Coma due to cerebral lesions:* In another type of cases, not commonly met with either, cerebral hemorrhage or softening is found at the autopsy. In these cases the coma is the result of the cerebral lesions.

3. *Acetonemic coma:* Finally, in another category of cases, which are relatively very numerous, the body is observed at the *post mortem* to give off an odor of acetone; the brain is rather pale and, in addition, there are also *rather often* kidney lesions. Such is the condition revealed in about 95 per cent. of all cases of diabetes that

have succumbed in a state of coma. I desire to lay special stress on the fact that renal lesions are rather often met with. While they occur only in a minority of cases, it cannot be asserted that, if uremia plays a part in the production of coma, that part is entirely subsidiary and conditional. I must also add that in a few quite rare cases lipemic thromboses have been found in the cerebral vessels. This complication is, however, of but little importance in view of its infrequency, and it may be definitely asserted that in the vast majority of cases it is the acetonemia alone which is the cause of the coma.

It is important to distinguish between symptoms due to the excess of sugar in the blood and those due to the acidosis. The difference in the effect of large doses of sodium bicarbonate in acidosis and in coma confirm the difference in their causal factors. Acidosis, due to acetonic bodies, is characterized by somnolency, vertigo, dyspnea, vomiting or diarrhea, etc., but coma shows other symptoms, muscular relaxation, loss of consciousness and disturbances in respiration, circulation and temperature. When in the course of progressive acidosis coma comes on suddenly, it never gives the impression of being an aggravation but a superposed complication. The two are closely associated, but they may possibly be due to intoxication by a different mechanism. Many features of coma suggest intoxication from polypeptids. M. Labbé (Presse méd., April 3, 1913).

Pathogenesis of Diabetic Coma.—The acetone bodies—especially beta-oxybutyric acid—possess a rather high degree of toxicity, which is but little inferior to that of lactic acid. According to Desgrez, the intravenous injection into rabbits of beta-oxybutyric acid in the dose of 1.6 grams per kilogram of body weight produces death. In the light of this result, a considerable amount of the acid would have to be retained in the system to cause death; but it may be that in the presence of chronic intoxication the resisting power is diminished. It is certain, at least, that the reserve of sodium in the organism is diminished. One can thus understand how the amounts of beta-oxybutyric acid found in the organs upon post-mortem examination of comatose diabetics were sufficient to bring about death. Magnus-Lévy reports having found as much as 1 gram of the acid per kilogram of muscle-tissue.

The writer emphasizes the importance of estimating the degree of acidosis as the only guide for proper treatment. It can be readily determined by gauging the amount of sodium bicarbonate which the patient must take in order to render the urine alkaline. By this simple means it is possible to obtain an instructive insight into the intensity of the acidosis, and thus to regulate the diet accordingly. He gives the tabulated findings in a few typical cases, with the amount of sodium bicarbonate on which the urine changed from an acid to an alkaline reaction. In one case, for instance, with 1.42 Gm. acetone and 7.8 total oxybutyric acid, only 10 Gm. of sodium bicarbonate was required to keep the urine alkaline, while in another case with the identical figures for the acetone and the oxybutyric acid, 25 Gm. of the bicarbonate was necessary to produce the same effect. Another patient with 9.5 Gm. sugar, 3.19 acetone, 24 butyric acid, and 29.8 total oxybutyric acid, required 30 Gm. of the bicarbonate. In another, a most remarkable case, the patient with 7800 c.c. of urine, 22.27 Gm. nitrogen, 180.9 sugar, 16.809 acetone, 30.24 acetone as oxybutyric acid, 96.36 oxybutyric acid, 126.6 total oxybutyric acid, and 5.34 ammonia, required 150 Gm. sodium bicarbonate before the urine gave a neutral reaction. With 110 Gm. the next day the urine became slightly alkaline, and with 80 on the third day the alkalinity became more pronounced. The urine continued alkaline as the amount of the bicarbonate was gradually reduced to 30 Gm. in the course of a week. In health, from 5 to 10 Gm. of the bicarbonate induces a distinct alkaline reaction, but in mild diabetes 20 Gm. are necessary, in the moderately severe 20 or 30, and the serious cases 50 Gm. and over. In the severest cases and in diabetic coma it is impossible to obtain an alkaline reaction. The writer warns that the carbohydrates should not be entirely withdrawn until the urine has been rendered alkaline. The method convinces the most skeptical, he says, as to the large amounts of sodium bicarbonate that may be needed in individual cases, and also as to the successful results when the proper dosage is reached. L. Blum (Jour. Amer. Med. Assoc., from Therapie der Gegenwart, March, 1910).

An extensive experimental research on coma by the writer showed it was possible to induce in rabbits a coma resembling so closely diabetic coma in man that a number of new and previously undescribed elements in the clinical picture could be elicited. He brought on the coma in the animals by administration of butyric acid (1-beta-oxybutyric acid and aceto-acetic acid). The butyric acid acts as a severe poison for the brain, affecting in particular the respiration center, vasomotor center, and the cerebrum. When the butyric acids act predominantly on the vascular system, a cardiovascular form of coma may be induced. The unmistakably favorable action of sodium bicarbonate in coma is due to its effect in stimulating the elimination of the toxic butyric acids through the urine and also to a direct stimulating action on the nerves of the vessels. The alkali is not able to cure existing coma, but it has proved its usefulness in aborting it when given early enough. The facts observed explain the origin of diabetic coma and show the importance of recognizing the action of the poisonous fatty acids on the respiration center in the peculiar low and deep breathing. This should warn of impending coma and permit treatment in time. The toxic action on the respiration center gradually extends to the rest of the central nervous system, with actual coma as the result. The assumption that the brain is predominantly affected by the butyric acid salts is sustained by the fact that in the experiments related the dose needed to bring on coma had to be proportional to the weight of the brain rather than to the entire weight. The small amounts of acetone found in the urine of the animals in coma exclude the assumption that accumulation of acetone is responsible for the development of diabetic coma. Ehrmann (Jour. Amer. Med. Assoc., from Berl. klin. Woch., Jan. 13, 1913).

It is possible, moreover, that the acetone bodies are not exclusively the toxic agents causing coma: Hugouneng and Morel have supposed that the products of cleavage of protein materials play a rôle in the causation of diabetic coma.

Acid intoxication in diabetic coma may be due to overaccumulation of acids, to a deficiency of alkalies, or to an insufficient output of acids to which the condition is due. Acidosis is much more common than is generally supposed. It is characterized invariably by increased breathing, and this may be a greater intake of breath at each respiration—hyperpnea—or an increase of the respiration. Lately it has become known that the respiratory center is particularly sensitive to acids, and that the respiration is a means of throwing off the excess of acid in the blood. This acid is mainly carbonic acid. On finding a patient in coma where no history can be obtained, with nothing to explain the coma on physical examination, hyperpnea denotes that the condition is one of acid intoxication. In this condition, alkalies are indicated. On the contrary, the absence of excessive action of the lungs serves to exclude acidosis from diabetes or other cause. Meat and other proteins should in such a case be excluded from the diet. While they do not actually cause acidosis, they surely tend to increase it, and should be kept down in cases of nephritis and diabetes that show any tendency to become comatose. Porges (Wiener klin. Woch., Bd. xxiv, S. 1147, 1911).

In certain cases of diabetic coma a condition of acute dehydration of the body tissues is responsible for some of the symptoms. Its existence is shown by the hollow facies, with sunken eyes and drawn features—Jaccoud's "peritonitic form" of diabetic coma,—sometimes associated with hiccough, vomiting, epigastric pain, and a frequent, readily compressible pulse. The skin is flaccid and inelastic. The facies differs from that of cholera merely in its roseate or cyanotic coloration. The blood-pressure and the intraocular tension are low, the latter, in one of the authors' cases, being in fact reduced from 25 mm. Hg. to 1 mm. Examination of the blood shows increased viscosity. While doubtless in part the result of vomiting, diarrhea, and polyuria, the dehydration is believed to be due chiefly to the polypnea (Kussmaul's dyspnea), which frequently occurs in diabetic coma and is likely to cause excessive loss of water through the lungs. From the therapeutic standpoint, the advisability is suggested of avoiding the administration of hypertonic alkaline solutions, which, while counteracting acidosis chemically, tend to increase dehydration of the tissues through osmotic action. Solutions approximately isotonic, *e.g.,* 1.5 to 2 per cent. sodium bicarbonate, should alone be employed. Chauffard and Rendu (Revue de méd., June, 1912).

Symptomatology of Acetonemic Coma.—The premonitory symptoms are of extreme importance, because of the fact that before coma appears some chance is afforded of preventing its occurrence by appropriate treatment. These premonitory symptoms comprise: (1) Certain urinary symptoms, viz., the presence of an abundance of acetone bodies in the urine, as well as of ammonia; often a diminution of the glycosuria because of the decrease in glycogenesis; diminution of the urea nitrogen as compared to the total nitrogen; copious cylindruria. (2) Acceleration of the pulse. (3) Headache. (4) Anorexia.

Ronchese's test for ammonia in the urine as index of diabetic acidosis is easily carried out. A 10 per cent. solution of sodium carbonate is added, a drop at a time, to the urine until the reaction becomes neutral. The formalin (40 per cent.) is neutralized with a one-fourth normal soda solution against phenolphthalein until a slight pink tint develops. Then 25 c.c. of the neutral urine and 10 c.c. of the neutral formalin are mixed and titrated against decinormal soda solution until a deep pink develops. The calculation is simple: 1 c.c. of the decinormal soda solution for 100 c.c. of urine corresponds to 0.017 Gm. ammonia in 1000 c.c. of urine. Marcovici (Wiener klin. Woch., July 21, 1910).

Next there appears a symptom which is a close forerunner of coma, viz., altered respiratory rhythm, generally characterized by an abnormal amplitude of the respiratory movements. This change of rhythm is not pathognomonic, greatly resembling that which occurs in uremia; but under the circumstances in which it presents itself, that is, those just referred to, it assumes very great importance.

If no treatment is resorted to, coma generally appears rather suddenly, and when it is once established, no sort of medication, with the exception, sometimes, of an intravenous injection, is capable of saving the patient. At this time there is usually noted a very peculiar lowering of the tonicity of the eyeballs, which indicates a decrease in the watery element of the tissues. Exceptionally, comatose diabetics may present convulsions; this occurs most frequently in cases where slight uremia complicates the acetonemia. Death takes place after an interval rarely exceeding thirty-six hours.

Organs of Special Sense.—Cataract is the most common symptom; it nearly always develops in both eyes, if not simultaneously, at least with but a short intervening period. It is characteristic of this form of cataract to be relatively soft. Retinitis is next in order, with white exudations along the vessels and in the perimacular region. According to Mauthner, many causes may lead to ocular lesions in this disease. Among them are (1) diminution of water; (2) diminution of resistance of the vessels, due to general weakening of nutrition; (3) the existence of a toxic substance in the blood, produced by abnormal processes; (4) various complications.

From a study of 25 cases in which ocular lesions of various character were found by Hirschberg in association with diabetes, three groups were distinguishable: (1) a characteristic inflammation of the central region of the retina, with small, bright areas, and frequently also small hemorrhages; (2) retinal hemorrhages, with the consequent inflammatory and degenerative changes; (3) rarer varieties of retinitis and degeneration, the relation of which to the constitutional disease remains to be demonstrated.

The retinitis is nearly always accompanied by slight hemorrhages. True optic neuritis is much more rare. According to Saundby, the retinitis of diabetes is distinguished from that of Bright's disease as follows: 1. The patches are irregularly distributed around the center of the retina, not specially near the macula, and are met with on the nasal as well as on the temporal side of the disk. 2. The patches are never arranged in a fan shape. 3. They are never associated with papillitis or diffuse retinitis. 4. The hemorrhages are, as a rule, punctiform, and not striated. 5. Hemorrhages into the vitreous are common.

A retrobulbar neuritis would explain the existence of the central scotoma sometimes met with in diabetes.

Besides the ocular lesions mentioned, Panas, and, after him, Hirschberg, have insisted upon visual disturbances caused by a defect of accommodation.

Out of 7176 eye patients by the last-named observer, 113, or 1½ per cent., were diabetics. After ten years' existence this disease regularly causes, he states, alterations of the eye structures, particularly the lens and retina. In a third of the cases diabetes then was found associated with some of the following significant changes: (1) uncomplicated paralysis of accommodation in middle life; (2) late myopia occurring between 40 and 60 years, without changes in the lens; (3) retinitis, and (4) quickly developing cataract in young persons in poor health.

There may be functional ocular disturbances with diabetes, either of refraction or visual acuity. There may also be partial paralysis of accommodation, probably toxic in origin, according to Terrien. Myopia is not uncommon; neither is cataract or diminished refraction, or there may be disturbed central or peripheral vision, amblyopia, hemianopsia, etc. Separate muscles may be paralyzed, and diplopia.

Paralysis of the intrinsic muscles

is very rare. Paresis of the abducens sometimes occurs; also a combined paralysis of the oculomotors giving rise to imperfect lateral motion of both eyes. A nuclear origin is evident in these cases.

Gellé states that suppuration of the *ear* is not rare in diabetics. The progress of acute otitis is the same as that observed in gout: rapid tumefaction, protrusion, and redness of the tympanum. During the second day severe pain appears, and later there is abundant suppuration from the external meatus.

> Changes occurring in the mucous cavities of the head and neck in diabetes are by no means uncommon. In the mouth, evidences of perverted nutrition are frequently found. The secretions become distinctly acid and act on the necks of the teeth, exposing the deeper and more sensitive parts to the ever-present infection in the mouth, hence spongy and bleeding gums and aching teeth are symptoms of importance in diabetes, the existence of which is often recognized by dentists from the mouth symptoms. Aphthous stomatitis, thrush; a large, red tongue, sometimes with black fur in the middle; hyperemia of the mucosa which often presents a glazed appearance and feels dry, are frequent symptoms. If acetone is present in quantity its odor is imparted to the breath and the patient himself may be aware of the sweetish taste. Sialorrhea has been observed in some individuals with pancreatic disease. In the throat there is dryness which is not to be confounded with pharyngitis atrophica. In the dry pharyngitis of diabetes the mucous membrane is usually red and glazed in appearance. This symptom is considered important in connection with others in the diagnosis of diabetes. O. J. Stein (Jour. Amer. Med. Assoc., March 26, 1910).

Inflammation of the mastoid has been observed in diabetes mellitus by R. A. Urquhart.

> There is something almost characteristic in mastoiditis in diabetes in that the mastoid is often attacked without any marked signs of trouble in the tympanum, beginning apparently as a primary ostitis; the destruction of bone takes place more rapidly and more extensively than in other cases. On the other hand, when an acute otitis media does precede mastoid inflammation, there will be, sometimes, an unusually small amount of pain, but the membrane will continue persistently bulging in spite of repeated incision. The lumen of the canal is apt to be narrowed, due to sagging of the walls, or to an external otitis, or to a furuncular condition to which these patients are prone.
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> Whether the destruction of the bone in the mastoid be rapid or slow, the acute inflammatory phenomena are apt to be absent until late; this would seem to indicate a low vitality or resisting power. This fact constitutes an additional indication for early operation. The postoperative condition of the wound would seem to bear out this question of low vitality of the tissues, as the granulations have a tendency to become large and flabby.
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> Speed in operating and short anesthesia are extremely important factors. B. H. Potts (Penna. Med. Jour., April, 1910).

Cardiovascular System.—The lesions of the heart have been, until recently, but indifferently studied. The organ undergoes a reduction in size and weight in about one-half the cases. In over one-third of the cases I have it hypertrophied. Mayer has also observed this, and states that increased cardiac volume, either from hypertrophy or dilatation, is much more frequent in diabetes than one would suppose from the literature, he having found it without other anatomical lesions in 82 out of 380 cases.

These patients are either possessed of very delicate constitution, with the heart action weak and irregular, or they are obese diabetics, with the face red or cyanosed, who present a strong cardiac impulse and signs of dilatation of the heart, either with or without atrophy. These patients are liable to die suddenly. Such cases should not be confounded with the true diabetic coma; moreover, they differ from the latter by the absence of acetonuria and by the suddenness of death. Very often it is after a voyage or fatigue of some kind that these patients fall into a state of collapse, with cold extremities; small, feeble pulse; a more or less rapid loss of consciousness, and death in a few hours.

We have already alluded to the above cases and also drawn attention to the existence of angina pectoris in diabetics,—although the latter complication appears to be in relation rather with gout than diabetes.

Arteriosclerosis is common in diabetics. Ferraro dwells particularly upon generalized endarteritis. According to him, the atrophic and necrotic lesions reported in various organs are due to this endarteritis. That true gangrene (excluding death from acute specific processes, which may occur in any subject and at any age) occurs in diabetic patients unaccompanied by such arterial disease as would of itself produce the gangrene, yet remains to be proved.

Edema, which is quite common in diabetes, is not always symptomatic of an affection of the heart. It may possibly be due to complication with Bright's disease; to a venous thrombosis, of which examples have been reported by Pavy, Gull, Dionis des Carrières, Leudet, Potain, and others. In most instances, as maintained by Widal, it is caused by a retention of the chlorides,—whence the indication for a chlorine-free diet in these cases.

Pulmonary Apparatus.—The most frequent complication in this direction is pulmonary phthisis. At least one-third of the cases of diabetes treated in the hospitals are admitted on this account. The lesions of diabetic phthisis are almost always those of bacillary tuberculosis. The exceptions met with are cavities following pulmonary gangrene, which, as has been remarked by some clinicians, do not yield the usual fetid odor. There may also occur ulcerations due to a fibrous ulcerative pneumonia (Marchand). Dreschfeld, Fink, and others have reported such cases.

> Evidence collected by the writer does not show that tuberculosis occurs more frequently in diabetes than in the general population at the same age. But two facts are noticeable: (1) the lowered opsonic index to the tubercle bacillus and a number of other bacteria in diabetes; and (2) the large number of cases of diabetes late in the course of the disease developing a very acute, extensive, and rapidly fatal form of pulmonary tuberculosis. Tuberculosis occurs more frequently in diabetes than in certain other chronic diseases. The frequency of tuberculosis in diabetes varies with a great variety of different circumstances. In the author's 25 collected autopsies on diabetic patients, 6 showed active pulmonary tuberculosis varying in acuteness and extent of involvement, and 1 showed adrenal tuberculosis without tuberculosis elsewhere. Out of 355 autopsies collected from the literature since 1882, including also the author's 25 cases, 138 (38.9 per cent.) revealed pulmonary tuberculosis, mostly in an acute form. In some structures, for example, the bones, the author could not find a single case of tuberculosis in a diabetic patient. When diabetes and tuberculosis are associated the diabetes can usually be shown to have been the primary disease. C. M. Montgomery (Deut. med. Woch., Nov., 21, 1912).

After phthisis, pneumonia is a serious complication of diabetes.

Pneumonia is rare in diabetes. In 700 cases studied by Bussenius only 7 cases of pneumonia were observed, not counting 1 case of bronchopneumonia and 5 of influenzal pneumonia. In none of these cases did the sugar disappear during the febrile period. It may begin like ordinary pneumonia. I have seen several such cases. The temperature does not differ from that usual in pneumonia, and the urine remains, notwithstanding the fever, at its usual level. There are also cases of rapid pneumonia, of which I have observed several. In the primary congestive period death may ensue in a few hours.

Digestive Apparatus.—The gums are usually red and tumefied. Dental alveoloperiostitis exists, as a rule, when the diabetes dates back several years. The teeth soon become loose in the alveoli and fall out, and dental caries is frequently present. In arthritic diabetes pharyngitis is often present, or, at all events, congestion of the pharynx, with the expectoration of bloody mucus.

Garel describes a form of pharyngitis symptomatic of diabetes or albuminuria. There is at first a slight difficulty in deglutition, a sensation of pressure in the throat, and a deposit of mucus which annoys the patient considerably. An examination of the throat shows the pillars of the fauces and the posterior portion of the pharynx to be reddened, the mucous membrane red, swelled, and frequently covered by a layer of glairy mucus. Freudenthal noted a diabetic ulceration of the throat. The ulcers have a tendency to increase in depth and extent, and are extremely painful. These ulcerations do not present any characteristic appearance or location.

The stomach is dilated in all cases of polyphagic diabetes. In the latter cases the digestion is *apparently* accomplished much more readily than one would suppose in view of the enormous quantity of food taken, but this is often only seemingly the case, as, notwithstanding the absence of symptoms of indigestion, the food is imperfectly dealt with. The hydrochloric acid is often absent in the gastric juice (Rosenstein, Gans, Hönigmann). Sometimes there are lesions of the mucous tract (interstitial gastritis, atrophy of the glands); in other cases no distinct lesions have been observed. Gans and Hönigmann claim to have found hyperacidity in certain cases.

The disturbances of the intestinal digestion are less known, because they are less accessible for investigation.

Among 140 diabetic patients Seegen found the liver enlarged in 28: about 20 per cent. Others have found a greater proportion of enlarged livers, but it is to be borne in mind that examinations made during life do not yield uniformly dependable results. The temporarily congested liver presents a greater volume and consistency than in the cadaver. The differences of opinion concerning the condition of the liver in diabetes are, in a measure, due to this fact.

In certain subjects attacked with severe diabetes, a brownish color of the skin, and especially that of the face, similar to that witnessed in Addison's disease, is observed. But, as stated under Etiology, such lesions are not, as a rule, a complication of diabetes, but occur concomitantly or before this disease.

Hanot and Chauffard published 2 cases of this kind in 1882. Cases were afterward reported by Letulle, Hanot and Schachmann, Brault and Galhard, Barth, and others. Upon section, the liver is found hard and distinctly and uniformly sclerotic, and microscopic examination shows the hepatic cells to be infiltrated with yellowish-brown or black granulations, while at certain points there are large black masses. The sclerotic connective tissue shows by its topographical distribution the existence of bivenous cirrhosis. In the portal spaces obliterative endarteritis is found, with networks of biliary pseudocanaliculi, masses of pigment, and remains of destroyed hepatic cells.

The liver is the seat of predilection for deposits of pigment, but the latter has also been found in the pancreas (Hanot and Chauffard), as well as in slight quantities in the kidney, and even in the heart. Finally, it may occur in the skin itself.

The quantity of iron chemically determined in the pigmented organs is variable: Quincke found in 1 case an enormous quantity of dry matter. The liver was said to contain, in all, 27 grams. Zaleski justly remarks that this pigmentation is not characteristic of iron.

Urinary System.—Urinary complications are very common. First there are those due to previous morbid conditions (gout, for instance), and, in particular, there are those which depend upon the diabetic dyscrasia, and which, as is known, are *complex* in the case of gravel diabetes.

The renal lesion most common in diabetes has been reported by Armanni and fully described by Strauss. It affects exclusively the zona limitans, where it invades the straight tubules of Henle, which may be either large or slender; sometimes, likewise, some of the collecting tubules (Strauss). As to the localization, there are individual variations; in one instance it was found exclusively in the ascending branch of the loop.

Armanni regarded this lesion as a hyaline metamorphosis. Ehrlich, with the aid of iodized gum, proved that it is really an infiltration of the cells by the glycogenic substance. He regarded it as a constant symptom in diabetes; but this opinion appears to be somewhat exaggerated. At all events, this lesion affords proof of the ease with which the organism synthetically transforms the sugar into glycogen. Ehrlich thought that the sugar so transformed was that contained in the urine. Strauss—basing his opinion upon the fact that the lesion is localized in the zona limitans, in the neighborhood of the capillaries interposed between the uriniferous tubules—is inclined to believe that this sugar comes from the blood of these capillaries. In support of this hypothesis the fact may be advanced that the glycogenic infiltration may take place in other organs besides the kidneys; the brain, for instance (Futterer).

In certain cases of severe diabetes, particularly when death has been caused by coma, Ebstein has seen a peculiar alteration in the epithelium of the convoluted tubules in which circumscribed areas alternate with normal portions. According to Albertoni, this lesion is due to the acetone or to the acids which exist in the blood in severe diabetes.

More recently, and only in cases in which death occurred during coma, Fichtner has reported a very circumscribed alteration in the cells of the convoluted tubules, which consists of an infiltration of fat at the base of these cells, which is detected by osmic acid. I have also met with this change, to which the attention of pathologists should be directed. In a study of 644 post-mortem examinations on subjects who had died of diabetes by Colcord, the condition of the kidneys was carefully noted in 241. In the remainder they were reported healthy, or only the gross appearances were noted. Of the 241 cases, 68 were noted as hypertrophic; 52 as hyperemic; 94 as the seat of a nephritis; 17 as having fatty degeneration; 7 had epithelial accumulation; 2 had cysts, and 1 multiple abscesses.

Lesions similar to those of Bright's disease rarely occur in the diabetic kidney.

> Albuminuria is a frequent development during the progress of diabetes, over one-third of all cases manifesting this symptom at some time during their course. It may be divided into two varieties—toxic and degenerative. Toxic albuminuria is generally of acute onset, arising during the later stages of the severe forms of the disease, as the result of irritation of the tubular epithelium, producing hyaline degeneration thereof, and due to the presence of acid toxins in the blood and urine. It is an invariable precedent and accompaniment of coma, and may be regarded as of the greatest prognostic significance. Degenerative albuminuria occurs with great frequency during the progress of the mild type of the disease, and is of renal origin and produced by a gradually developing nephritis, which arises from prolonged hyperfunction and impairment of renal nutrition. The appearance of albumin under these circumstances, while of little immediate significance, is of the greatest eventual importance, as indicating the intrusion of chronic nephritis into the already manifold clinical difficulties. Elliott (Jour. Amer. Med. Assoc., Aug. 8, 1903).
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> In the last stage of severe diabetes, and in diabetic coma, albumin is nearly always present. This albumin is never very considerable. Renal changes have been found by various observers. Frerichs and Ehrlich found the principal changes to be a glycogenic degeneration of Henle's loops, but, according to others, a hyaline degeneration of Henle's loops and the straight tubes. Ebstein has described necrosis of the epithelium of the kidney, which, he considers, is produced by toxic substances such as acetone, diacetic acid, etc. However small, short hyaline, and finely granular casts are demonstrable. Richard Jones (Austral. Med. Jour., Oct. 12, 1912).

Several authors have dwelt upon the frequency of *cystitis* in diabetic subjects.

A complication which is much more rare is *pneumaturia,* in which the patient toward the end of micturition ejects a jet of gas through the urethra. In a patient observed by Mueller, the gas, which was collected under water, was composed as follows: H, from 44 to 57 per cent.; N, from 33 to 35; CO_2, from 9 to 19; O, traces; CH_4, traces. Freshly voided urine contained 1 per cent. of sugar, but sometimes there was no trace of it. There is no doubt that the fermentation of the sugar in these cases is due to the presence of micro-organisms in the bladder.

Skin. — The cutaneous complications occurring in diabetes are pruritus, eczema, and gangrenous lesions. The pruritus may exist without any appreciable lesions. It affects the genital organs, especially the glans penis in men. In women it is much more painful, affecting the vulva. It gives rise to an itching, burning sensation, with exacerbations, which may cause insomnia and various nervous symptoms. Sometimes it occurs early and is one of the symptoms first revealing the existence of the disease.

Diabetic eczema is of two varieties: either genital, in which case, like the pruritus, it appears to be due to the local irritation caused by the sugar, or general, when it occurs principally in arthritic subjects. Chronic eczema of the genital organs in women may be pachydermic (Fournier).

The gangrenous dermatoses have been carefully studied by Marchal de Calvi, and more recently by Kaposi.

Furuncle and carbuncle frequently complicate diabetes. The carbuncle presents a somewhat peculiar type, beginning insidiously, and with but little pain; edema is not marked, and the febrile reaction is either slight or does not exist. Very frequently the affection is complicated with a phlegmonous process or with gangrene.

Gangrene may be primary in diabetics, without any previous phlegmon or carbuncle. In this case it is dry or mummified, like senile gangrene. It begins most frequently in the toes, and has been seen to originate simply in a local asphyxia. I have already mentioned the diabetic perforating ulcer. (See Nervous Complications.)

A form of lichenoid exanthema has been described in diabetes. In a patient seen by Robinson touching the tumor caused a burning sensation. Grube observed 9 cases in which psoriasis coexisted with gout, or diabetes, or both; this writer holds that a causal relation between those affections does undoubtedly exist.

Sherwell enumerates the cutaneous disorders observed in diabetes as follows: Generalized xeroderma, which is quite common; eczematous dermatitic manifestations occurring in any region of the skin, especially prone to attack the flexor surfaces, and more especially the genital, anal, and inguinal regions; furuncular and carbuncular manifestations are quite frequent in this condition, and are found generally in the nuchal and gluteal regions; erythematous lesions, some evanescent, others of the graver kind, as erysipelas, are commonly present; gangrene; dermatitis herpetiformis of Duhring; xanthoma diabeticorum; blastomycetic dermatitis.

Locomotor Apparatus.—The cartilages may present the lesions upon which Krawkow dwells, which are due to a deposit of glycogen.

Frerichs refers to the lightness of the bones. They have been found to be extremely light in some cases. I have stated above that in serious cases the lime in the urine is relatively increased. Perhaps these anomalies bear less relation to the hyperglycemia than to the acid dyscrasia of the severe form of diabetes, to which we shall now refer.

Concomitance of Diabetes and Cancer.—It is not an extremely uncommon occurrence for a cancer to appear in diabetics, and the observation is said to have been made that cancer runs its course more rapidly in these patients than in non-diabetics. A rapid course is not, however, constant in cancer occurring in diabetes.

Traumatism in Diabetics.—Wounds heal more slowly than normal in diabetics. Verneuil has compared them in this respect to alcoholics. As for the converse relationship, *i.e.*, an influence exerted by trauma upon the course of diabetes, it is clearly shown in certain cases.

Concomitance of Diabetes and Febrile Diseases.—Febrile affections sometimes favor and at other times tend to prevent glycosuria, according to the nature and virulence of the infection present. Certain it is that a moderate degree of hyperthermia, not of infectious origin, reduces glycosuria by increasing the destruction of glucose. But on the other hand, clinical observations show positively that a pronounced infection favors glycogenesis by increasing the catabolism of protein substances.

Diabetes and Pregnancy.—Spontaneous abortion is observed to occur rather frequently in diabetic women. At all events, the product of conception comes to term only in two-fifths of the cases. The surviving children, moreover, generally do not enjoy very sound health.

As for the influence exerted by pregnancy on diabetes, it is rather prejudicial than otherwise; but there are exceptions to this. It is difficult, indeed, to formulate any useful generalizations on this point. Each case must be considered individually.

The writer's personal experience and study of 55 papers bearing on the subject, showed that diabetes is an extremely dangerous and unfortunate complication of pregnancy, both for mother and child; the outcome is never certain. Even after sacrificing the life of the child, it is always doubtful whether the mother can recuperate. Whether or not to deliver the woman at once must be decided for each individual case, but if the decision is in favor of it, there must be no further delay. General anesthesia should be avoided in such cases, but possibly spinal or scopolamin-morphine anesthesia might take its place. Offergeld (Zeit. f. Geb. u. Gynäk., Bd. lviii, Nu. 2, 1906).

The writer's experience and observation have demonstrated that the coincidence of pregnancy and diabetes is extremely rare, and also that neither seems to have a specially harmful influence on the other. He advises examining the urine of every pregnant woman for sugar, even in the absence of symptoms. This is the only certain way to detect glycosuria in its incipiency. Dietetic measures should be rigorously enforced from the start until delivery, but the pregnancy should never be interrupted on account of the diabetes alone. Treatment should be exclusively dietetic. In 285 cases of fatal coma reported by four French or German clinicians, 36 of the patients were between 20 and 30, and 77 between 30 and 40, with 19 under the age of 10. Fatal coma during pregnancy occurs in a smaller proportion than the general average of coma in diabetes. On the other hand, from 20 to 25 per cent. of pregnant diabetic women develop tuberculosis. In 6 cases previously reported by the writer, subjective symptoms were not complained of in any instance, but all the patients, even in the mild forms, were thin, languid and moody, and looked badly. The pregnancy and puerperium were normal and the children were all well developed and thriving, with the exception of one child, who weighed only 4 pounds; both parents were diabetic. Sugar was found for a few days in the urine of the infant of one mother with severe diabetes. The vital indication in treatment is to insist on a strict antidiabetic diet, interposing occasional days of fasting and of exclusive vegetable diet, commencing this at the earliest possible moment and keeping it up through the puerperium. The benefit was manifest in his experience—no fatalities and fine, healthy children. No anesthetic should be given, and the woman should not get up for two weeks after delivery; reading and visits should also be discouraged. Women with an inherited or acquired diabetic taint should not nurse their children, as the diet generally taken by nursing women might rouse the dormant tendency, or aggravate existing diabetes. Neumann (Jour. Amer. Med. Assoc., from Zeit. f. klin. Med., Bd. lxix, Nu. 5-6, 1910).

COURSE. — While essentially a chronic affection, diabetes may exceptionally occur in an acute form. Authentic cases of this nature are rare, because the evolution of the disease may actually have been an incipient one, and have remained unnoticed up to a certain period, when there is a sudden aggravation.

[Loeb reports the case of a chemist who, while in good health, examined his own urine and found it normal. Soon after he became ill, and experienced violent thirst. At this time the urine contained 8 per cent. of sugar. Death took place in five weeks.]

Death is not invariably the termination of acute diabetes. Several cases of recovery have been reported. Holsti saw, in a man 41 years old, diabetes having a very sudden beginning, judging by the thirst, and which was only subjected to dietetic treatment six weeks later. After three days of abstinence from amylaceous food the urine, which had contained 8.8 per cent. of sugar, lost all trace of it, and the subsequent use of starchy food did not cause a return of the diabetes. This is, of course, a rare case. More frequently a diabetes having an acute beginning passes into a chronic condition.

A mild form of diabetes has sometimes been described as *intermittent;* it is due in a measure to the influence exerted by a too liberal diet. As soon as a proper diet is instituted the glycosuria disappears. This is not, properly speaking, an intermittent diabetes. Such cases belong rather to the type of alimentary glycosuria. In a series of 6 cases of recurrent transitory diabetes studied by Dreyfus Brissac, the proportion of sugar was very variable, but usually 30 to 40 g. a day. The glycosuria diminished rapidly under a rigid diet. The amount of sugar was generally less in the second and third attacks than in the first, but the attacks lasted longer with each relapse, 1 or 2 g. of sugar persisting for weeks or months. As a rule, there was albuminuria, which subsided with the glycosuria. The proportion of uric acid was high. In all cases there was a moderate degree of polyuria. Thirst and hunger were never marked, but emaciation, a sense of physical exhaustion, and depression were prominent symptoms; these recurred with diminished intensity with each attack. Months or years of perfect health sometimes separated the attacks. In 1 case ordinary diabetes supervened. The recurrent transitory variety of diabetes is connected in certain cases with a constitutional arthritism, in others with an acquired arthritic tendency.

Transitory diabetes is not dangerous in itself; it is the expression of an enfeebled constitution or a transitory dyscrasia.

True intermittent diabetes is almost independent of the alimentation. Cases of this variety have been reported by Bence-Jones, Baudremont, and others. Saundby reports 1 case. I have myself seen 1 alternating with albuminuria. This form of diabetes is principally met with in arthritic and hysterical subjects. Its appearance depends principally upon nervous causes, mental or otherwise.

DIAGNOSIS.—A well-defined diabetes cannot be mistaken by an experienced physician. The general symptoms and the glycosuria establish the diagnosis.

Diagnosis by Examination of the Urine. 1. Is there sugar in the urine? If the percentage of sugar found in the urine is considerable, no doubt is possible. If, on the contrary, a minimal quantity is found, there is some room for doubt. Where only a trace of sugar is present, indeed, its presence may be overlooked by the physician; for if it is tested for with Fehling's solution, and there happens to be a rather high percentage of creatinine in the urine, the latter substance, by virtue of its basic nature, will keep in solution the small amount of oxide which should have precipitated. The proof of this as a possible source of error may be had by adding to the urine of a normal individual eating freely of meat a small proportion of glucose (about 2 Gm. to the liter): It will be impossible to recognize the presence of the latter with the copper test, whereas, if the same proportion of the sugar were dissolved in pure water and tested for, its presence and relative amount could be determined with absolute correctness.

A more common mistake, however, is that of believing to recognize glucose, when none is present: One not infrequently meets with more or less obese arthritics who present the appearances of diabetes excepting that the amount of urine voided is small. If they are heavy eaters, as is often the case, their urine will contain a large amount of uric acid and other reducing substances, so that an inexperienced examiner will readily believe the reduction observed in the test to be due to sugar. The decision is, indeed, at times a rather difficult one. Following is the method of attaining it: If the urine contains at least 3 Gm. of sugar to the liter, Nylander's reagent may be used, which consists of a solution of bismuth subnitrate and Seigrette salt in 10 per cent. sodium hydroxide; 10 parts of urine are boiled with 1 part of the reagent for two minutes, when, if sugar is present, a blackish discoloration of the fluid makes its appearance. The oxide of bismuth possesses over that of copper the advantage of not being reduced by uric acid, creatinin, etc.; but it is essential that from the urine used all albumin and mucin have previously been removed, since a trace of albuminous matter will blacken the fluid owing to the formation of bismuth sulphide. In case of doubt, the fermentation test should be tried, and especially the urine referred to a chemist, who will determine whether an osazone can be made from it.

Where no chemist is available, the physician should proceed as follows: In non-albuminous urine deprived of the greater part of its uric acid by preliminary cooling (on ice) and by filtration, sugar may be considered present if the reduction of the cupro-potassic fluid takes place in the cold state, as the reducing substances only exert their action at the boiling point. Sugar itself, in the cold state, only causes a reduction at the end of several hours.

If one does not wish to wait, recourse may be had to the following process, which is a modification of that proposed by Worm-Mueller, to determine whether the reduction by heat is partially due to a small quantity of sugar: The exact quantity of urine required to decolorize 1 c.c. of Fehling's solution must first be determined; then a portion of the same urine is fermented. This having been accomplished, it must then be ascertained whether a greater number of cubic centimeters will be required to decolorize the same quantity of Fehling's solution.

It is clear that if a larger quantity is required a portion of the reducing power was due to the presence of a certain amount of sugar. This method is exact, and its only defect is that it is not within the reach of the ordinary practitioner, owing to the precision required in the determinations.

> Certain mistakes must be avoided. The sugar test may fail unless a twenty-four-hour sample is taken, and it may disappear and be replaced by uric acid and phosphates. The turbidity of diabetic urine is noticeable and it is of practical importance, as it is due to the growth of yeast cells which may cause, by fermentation, complete disappearance of glucose if the qualitative and quantitative examination is not made sufficiently early. Many other substances than glucose will reduce the various copper solutions, among which may be mentioned, as most frequent, conjugated glycuronic acid, alkapton creatinin, uric acid in excess, blood, and lactose. A point that the writer has not seen mentioned elsewhere is that occasionally the urine of menstruating women will reduce the copper solution, on account, as he is fully convinced, of the presence of blood in the urine. This is an important point. Blocking of the secretion of the mammary glands may also produce lactose in the urine, and the fermentation test will reveal the difference. It is surprising how easy it is to eliminate the above-mentioned reducing substances by the simple Fehling test provided it is properly done, *i.e.,* after boiling the solution and adding the urine drop by drop. Reboiling is not necessary, warming will do. If the reduction is rapid we may be pretty certain of the presence of glucose, but if it is slow and the precipitate yellow, instead of red, the fermentation test will verify. W. Lintz (Jour. Amer. Med. Assoc., March 12, 1910).

To lessen the error due to the reducing substances, it has been advised to dilute the urine to one-fifth and even to one-tenth. Indeed, this should always be done when the urine is highly charged with sugar; but when there exists only doubtful traces of it, dilution of the urine becomes positively a cause of not being able to detect the sugar. This process should consequently be rejected.

On the other hand, the following method, which is, moreover, a classical one, is perfectly reliable: About 4 Gm. of Fehling's solution are poured into a tube; this is heated to the boiling point, then 1 to 2 centiliters of urine, non-albuminous, which is supposed to contain sugar, should be made to flow along the side of the tube, which should be slanted. It is well to first heat the urine slightly; or, the inclined tube may be held above a flame for a few moments in order to raise the temperature sufficiently at the point of contact of the two liquids. After a few moments, if sugar is present, a green ring will be seen to form, which will then rapidly change to yellow, and afterward to red, the latter contrasting decidedly with the blue color of the subjacent liquid. This reaction is easily carried out, and, if a red ring is obtained, it is of great value, for the other reducing substances only produce hydrate of copper, which is of a yellow color.

Jastrowitz has advised the examination of the precipitate of oxide of copper under the microscope. It is a fact that none of the reducing substances, uric acid, creatinin, nor the compounds of glycuronic acid, etc., produces a crystalline precipitate. According to the author, the copper oxide crystals are tetrahedral and octahedral. These are actually the forms obtained when a watery solution of glucose is made to react upon Fehling's solution, but, according to Jastrowitz, small spheres may also be produced with urine containing a slight amount of sugar. Thus, when, under the microscope, these (spheres) predominate, provided they are accompanied by tetrahedral and octahedral crystals, it may be affirmed that sugar is present in the urine.

It is possible partially to get rid of the reducing substances by means of a process described a long time ago by **Seegen**, and which is to be recommended on account of its simplicity. The urine is filtered through animal charcoal as many times as is necessary to decolorize it; the charcoal is then washed in distilled water, and the two filtered liquids—the urine and the distilled water — treated separately with Fehling's solution.

The purpose is as follows:—

The charcoal not only retains the coloring matter and the uric acid, but likewise certain substances, as yet not well known, which prevent the precipitation of the oxide of copper. Therefore one is better able to search for the sugar with the filtered water than with the urine. Furthermore, the charcoal has retained a large portion of the sugar contained in the urine, and gives off into the distilled water a larger portion of the sugar than of the other substances which it had retained. Consequently the reduction of Fehling's solution is much more easily accomplished by this water than by the urine.

These are the advantages of Seegen's method, by means of which the author has been able to discover a one-thousandth part of sugar in the urine. Even with a smaller proportion there will be a reaction, but this will only become apparent, according to Seegen, after several minutes' heating. No other method surpasses this in sensitiveness, and it is most easy of application, *provided a perfect animal charcoal is available.*

To summarize what I have already stated in the beginning, Fehling's solution, provided one knows how to use it, is capable—all statements to the contrary notwithstanding — of alone determining the existence of sugar. The reducing action of glucose upon the oxide of bismuth in the presence of an alkali has also been resorted to for a long time. This reaction, called that of **Böttger**, which is described in all the treatises on urology, is far from being valueless, especially when made use of with the modification indicated by Nylander.

Leaving aside several other reactions, which have not come into general use because they are not sufficiently accurate, I pass on to the phenylhydrazin test, described by **Fisher**, and employed by von Jaksch for the discovery of glucose in the urine. This reaction is based upon the property, peculiar to phenylhydrazin, of forming when in combination with glucose a crystalline substance of a bright-yellow color.

Von Jaksch performs this reaction as follows: 10 c.c. of the urine to be tested are poured into a tube, 3 pinches of crystalline sodium acetate added, and also 2 pinches of phenylhydrazin hydrochloride. The mixture is placed for a time in a water bath. After it has cooled, a yellow, crystalline deposit is formed, which, under the microscope, appears to be composed of fine needles, some isolated, others in agglomerations, and some assuming star formations.

It has been said that this reaction is not absolutely characteristic, and that glycuronic acid will also cause needle formations; but Hirschl has ascertained that upon leaving the tube one hour in the water bath the glycuronic compounds do not give rise to a crystalline precipitate, and Binet, who has made a very complete study of this important reaction, considers it as absolutely reliable with the following slight modifications: 10 c.c. of the urine to be examined, deprived of albumin, are taken and cleared by means of a few drops of an acetate of lead solution. The liquid is then filtered, and a few drops of acetic acid, 3 pinches of sodium acetate, and 2 of phenylhydrazin hydrochloride are added. The whole is left in the water bath for one hour. The tube is then allowed to cool, and on the following day the urine is examined with a powerful magnifying glass. Under these conditions no balls or granular masses are found, but yellow or silvery crystals, characteristic of phenylglucosazone. According to Binet, by proceeding in this way, one two-thousandth of sugar is distinguishable — an exceedingly small proportion. The reaction, which is absolutely correct, is, therefore, an extremely sensitive one.

I do not believe that the fermentation test is superior to it in this respect. Beer yeast alone, and likewise the urine itself, when left undisturbed, gives rise to gas-bubbles. Thus, in order to arrive at the certainty of the existence of the sugar, a test experiment must be made. Two similar test-tubes are prepared, the suspected urine is placed in one, and normal urine in the other, an equal quantity of yeast is added to each one, and they are left under the same conditions for twenty-four hours.

> The fermentation specific gravity method gives results as good as do the other methods. It is very simple in application, requires no laboratory equipment, and involves a mineral cost for apparatus. All that is required is to take the specific gravity of the urine at room temperature, add a small bit of commercial yeast and put in a warm place, such as an incubator at 37° C. 98.6° F.), a heated room, near a stove or radiator, etc. Active fermentation soon begins and is evinced by bubbles and currents in the urine. When fermentation is finished the specimen partially clears and the evolution of gas ceases. A negative test with Fehling's or Nylander's solution proves the end of the process—twelve to eighteen hours is usually sufficient. The specimen is now allowed to return to the room temperature of the previous specific gravity determination, and the specific gravity redetermined. The difference between these two readings, multiplied by 0.23, gives the percentage of fermentable substance expressed in terms of glucose. Christian (Boston Med. and Surg. Jour., Aug. 8, 1907).

To recapitulate, Seegen's method with Fehling's solution, the phenylhydrazin reaction, and the fermentation test are the three methods capable of detecting with certainty the presence of a small quantity of sugar. The first is by far the most rapid. The phenylhydrazin test requires at least two hours and the fermentation test twenty-four hours. A new test has recently been recommended by Benedict. (See also the article on GLYCOSURIA, this volume.)

The **Benedict test** for sugar is carried out with the following solution:—

Copper sulphate (pure crystallized)	17.3 Gm.
Sodium or potassium citrate	173.0 Gm.
Sodium carbonate (crystallized	200.0 Gm.
Distilled water ....ad	1000.0 c.c.

The carbonate and citrate are dissolved in about 700 c.c. of water with the aid of heat and the mixture poured in a large beaker. The copper salt is dissolved in about 100 c.c. of water and poured slowly and with constant stirring into the first solution. The mixture is then cooled and diluted to 1 liter.

This solution may be kept indefinitely in uncolored or cork-stoppered bottles. For use, 5 c.c. of the reagent is placed in a test-tube and from 8 to 10 drops (not more) of the urine added. Heat to boiling for two minutes and allow to cool. If glucose is present the entire body of the solution is filled with a precipitate, which may be red, yellow or greenish in tinge. If the amount of glucose is small the precipitate forms only on cooling. If no sugar is present the solution remains clear or shows a faint blue turbidity. S. R. Benedict (Jour. Amer. Med. Assoc., Oct. 7, 1911).

2. Is the Glycuria Observed a Symptom of Diabetes? The presence to a certainty of sugar in the urine does not alone warrant the diagnosis of diabetes, for the sugar present may not be glucose.

Lactosuria.—The sugar-containing urine of a woman in whom lactation has just been suddenly brought to a close, and which consequently contains lactose, might be mistaken for a diabetic urine; but the attendant clinical circumstances generally suffice to prevent such an error. Lactose, we may add, does not ferment with yeast.

Alimentary Pentosuria.—I have had occasion to examine a specimen of urine which, judging from its reducing power, appeared to contain several grains of glucose; but it had no rotatory power. The urine was that of a healthy individual who had partaken a few hours before of a large dish of white onions from the south of France. Its reducing power was due to a pentose (inactive arabinose).

Constitutional Pentosuria. — Pentosuria is not invariably of alimentary origin. In recent years a few cases of idiopathic pentosuria have been reported. This is a nutritional disturbance which is quite distinct from diabetes, in general not serious, but sometimes associated with nervous phenomena. It is necessary to distinguish it from diabetes even from the practical standpoint, since the customary antidiabetic diet is injurious to these patients.

Method permitting the detection of traces of pentose in urines containing a high percentage of dextrose. In urine with 5 per cent. of dextrose or less, 4 Gm. of phenylhydrazine hydrochloride and 8 Gm. of sodium acetate are added to 100 c.c. of urine, and the whole is heated for an hour over a boiling water bath. It is then well cooled, and the precipitate filtered off and placed in a beaker. Fifteen c.c. of hot water is added, the beaker is placed in a boiling water bath for five minutes, and the contents are then filtered. The filtrate is then distilled from a 400 c.c. distilling flask, the side outlet of which is cooled as in the ordinary Liebig condenser. Before heating, 6 c.c. of concentrated hydrochloric acid of specific gravity 1.19 is added and the upper outlet of the flask is closed with a rubber stopper. Six c.c. of fluid is then distilled off. To 3 c.c. of the product is then added 5 c.c. of Bial's reagent (1 Gm. of orcin dissolved in 500 c.c. of 30 per cent. hydrochloric acid, together with 30 drops of the official aqueous solution of ferric chloride), and the mixture is boiled for a short time. In the presence of only 0.05 per cent. of pentoses a distinct green coloration will appear. Where the urine tested contains 5 to 10 per cent. of dextrose, the amounts of phenylhydrazin and sodium acetate used should be doubled. Jolles (N. Y. Med. Jour., from Zentralbl. f. innere Med., July 13, 1912).

Levulosuria.—The polariscope also permits of the recognition, when the occasion presents, of levulosuric diabetes. This variety of diabetes is extremely rare.

Non-diabetic Glycosurias.—The well authenticated presence of *glucose* in the urine is not sufficient to warrant the assertion that diabetes exists, for various toxic effects or nervous influences, etc., are capable of giving rise to a temporary glycosuria. Where, however, the proportion of glucose exceeds 10 Gm. to the liter, it may be definitely stated that the condition present is diabetes.

[Thus, a woman of 45 years was once brought unconscious to my clinic. Three days before, she had been apparently well, but in the evening exposed herself to a draught of air while perspiring and experienced a chill, followed by headache, restlessness, and delirium. Since the preceding day she had been comatose. The interne, thinking the condition to be uremia, as the urine removed by catheterization contained albumin, practised venesection, which brought about no improvement in the patient's condition. She died two hours later. The urine was found to contain, in addition to a small proportion of albumin, 12.5 Gm. of urea and 24.7 Gm. of glucose to the liter. The autopsy revealed a suppurative cerebrospinal meningitis and a normal condition of the other organs, including the pancreas.

Was this a case of diabetes or one of symptomatic glycosuria in meningitis? In view of the intensity of the glycosuria I decided in favor of diabetes, and information obtained later from the husband showed that since two years at least the patient had been getting up several times each night to drink and pass water. It is therefore certain that this woman was afflicted with diabetes. R. LÉPINE.]

3. Diagnosis of Pathogenic Factors in Diabetes.—It is not enough to recognize the presence of diabetes mellitus; it is also important to find out what sort of a diabetes is present.

Since the disease is almost always the result of a combination of several pathogenic factors, it is necessary to determine, if possible, the relative importance of the factors present. Each individual case has therefore to be subjected to a minute analysis, in which are taken into account heredity, the habits as to hygiene, diet, previous diseases experienced, as well as the signs present at the time. In spite of the greatest care in conducting this investigation, information as precise as would be desirable will not always be obtained.

At first sight, it would seem relatively easy to recognize a case of pancreatic diabetes. As a matter of fact, this is often quite difficult, as the signs of pancreatic disease are ambiguous. It is not even easy to assert that there is a deficiency in the external secretion of this organ, unless a painstaking examination of the feces reveals simultaneously an abundance of fats, persistence of muscular nuclei, and deficient amylopsin, in which case hesitation is hardly possible. But even in this event no very significant information has been gained, as there is no certainty that the pancreatic internal secretion is likewise deficient. Conversely, if there is evidence favoring integrity of the external secretion, no reason is available for asserting that the same holds good with the internal secretion.

The writer records some interesting observations on the urine of diabetics. He studied 9 cases, in 7 of which there was a marked polyuria. In 8 cases of the 9 the cryoscopic figure was unusually high, while the difference between the total molecules excreted and the molecules of sodium chloride excreted was considerable. This showed that there was an excessive number of metabolic molecules elaborated by the kidneys, and that the renal epithelium was under a strain of overwork. This is necessary in view of the overproduction of effete materials in diabetes. In some cases the work of the kidneys as measured by cryoscopy was found to be four or five times the normal standard. Another interesting result of his observations was that so long as the relation between the freezing point of the urine and the blood remained the same, the patient's condition was fairly good. When the strain on the kidneys began to tell and when the concentration of the blood began to become more marked, the patient became comatose. Zimnitzki (Roussky Vratch, Oct. 7, 1906).

PROGNOSIS.—Most laymen appear to harbor a wrong impression of the seriousness of diabetes: Some think of it as a condition that can easily be neglected, others as an exceedingly grave affection. Except in the event of grave complications, the second of these ideas is no more reasonable than the first: Uncomplicated diabetes is a disease which, all else being equal, shortens life, but which, rationally treated, does not implicate an early fatal termination, and can often even be recovered from. Personally, I have had under observation for several years diabetics who might pass as having been cured.

The hopefulness toward the issue of this disease has in many cases been replaced by a pessimism. This is unwarranted by the facts in our possession. Success in treatment consists in attention to minute detail, in convincing the patients of our ability, and an endurance of hardships on the part of the patient. The knowledge that one-fourth of all diabetics might live ten years or more should be an incentive to good work. The adoption of early treatment is important. Occasional very long duration of life is noted. The writer reported the case of one such who was 80 years old, and had diabetes for twenty years, who was still alive. T. C. Janeway (Amer. Med. Assoc. Trans.; N. Y. Med. Jour., June 8, 1912).

There is therefore some ground for being surprised that the life-insurance companies should deal so severely with diabetics. Many of these cases have rather good chances of surviving, provided they will consent to have themselves treated. Indeed, lack of enlightened treatment, except in a few cases of transitory traumatic diabetes, inevitably results in aggravation of the disease.

Cases illustrating prolonged duration under appropriate diet without drugs:—

Case I.—Mild diabetes (glycosuria) in a man, with onset when aged 33 years, who became sugar-free, and remains so after fifteen years, upon a diet containing 125 Gm. carbohydrate.

Case II.—Moderately severe diabetes in a man, with onset when aged 50 years, who, when aged 66 years became sugar-free, and succumbed to arteriosclerosis and Bright's disease at 70, without return of sugar in the urine.

Case III.—Moderate diabetes in a woman with onset when she was aged 60 years, who after thirteen years upon a restricted diet maintains unusual physical and mental vigor.

Case IV.—Severe diabetes in a financier, with onset when he was aged 40 years, undiagnosticated for four months, but later treated with extreme care and complete co-operation on the part of the patient. Duration eight and one-half years.

Case V.—In contrast—severe diabetes with *diabetic heredity* in a bank clerk, with onset when aged 37 years. He gave up the opium treatment with despair some months after onset, and under a closely restricted diet for eighteen months, and later, upon a moderately restricted diet, lived twelve and one-half years.

Case VI.—Severe diabetes in a boy, aged 14 years, who lived three years and eleven months.

Case VII.—In contrast—severe diabetes with *diabetic heredity* in a girl, aged 17 years, who withstood the disease twenty-one years.

Case VIII.—Moderate diabetes occurring in a woman when aged 47 years (perhaps earlier), who successfully withstood the removal of an immense fibroid tumor, and is comfortable at 53.

The treatment of these patients had as its main object the removal of sugar from the urine by dietetic measures, provided weight and strength could be maintained. Usually a diet containing 100 to 150 grams carbohydrates was given at the start, and gradually the carbohydrates were lowered until the sugar disappeared from the urine. Vegetable days were freely employed and occasionally oatmeal days. E. P. Joslin (Amer. Jour. Med. Sci., April, 1913).

The prognosis of diabetes therefore differs greatly according to the case, the pathogenic factors that have operated in its causation, the age of the patient, his submissiveness to the regulations imposed by the physician, etc. The relatively great severity of diabetes in the young cannot be too strongly emphasized. Recovery from diabetes in the child is extremely rare. Again, according to Laache the prognosis is much more unfavorable in women than in men, especially during the period of life comprising the years between 20 and 30. This assertion, however, requires confirmation.

In his experience with 122 cases of diabetes only 22 per cent. of the 77 male patients died, while 40 of the 45 cases in women terminated fatally. This greater mortality among the women may be due to the fact that diabetes seems to affect preferably young women, and it is well known that the disease runs a more malignant course in comparatively young subjects. Laache (Med. Klinik, March 27, 1910).

The statement was already made, in regard to the diagnosis, that it was generally quite difficult to ascertain definitely the part played by each etiological factor in the causation of diabetes. It is accordingly, as a rule, impossible to give an accurate prognosis when a case of diabetes is first seen. Such a forecast can, however, generally be made after a period of observation. If the patient submits with scrupulous exactness to various diets, information will promptly be secured concerning his powers of assimilation in regard to the carbohydrates and even, in certain cases, concerning the intensity of the glycogenetic process.

Statistics show that the death rate from diabetes mellitus in England and Wales is steadily increasing. From the annual reports of the registrar general we see that the death rate from diabetes mellitus in England and Wales, in 1866, was 32 per million living; in 1866, 59; in 1906, it was 97. Taking the records for the last twenty years, we find that, in 1887, there were registered 1750 deaths from diabetes mellitus; in 1906, 3342. The death rate from the disease per million living increased from 63 in 1887, to 97, in 1906. The increase was seen in both males and females. In 1887, the death rate from the disease in males was 75 per million living; in 1906, it was 104 per million. In females, the death rate from the disease per million living was 51 in 1887, 90 in 1906. The risk of the disease is greater after 30 years of age. In 250 private patients the writer found 45 under 30 years; from 30 to 40, 30; 40 to 50, 60; 50 to 60, 72; 60 to 70, 38; 70 to 80, 5. Among the Jews diabetes is much more frequently met with than among Christians. The highest death rate is among publicans. Among jurists it is "three times the average, and higher than in any other occupation in the list, except innkeepers." Among medical men the mortality is also high. The mortality among chemists and druggists is high, but is less than among medical men. In occupations in which there is great mental worry, mental strain, or excitement, there appears to be an increased risk of diabetes developing. Williamson (Pract., April, 1909).

To the question, Can diabetics be allowed to marry? I believe it is proper, in general, rather to give a negative answer. If the patient is a young girl, pregnancy cannot be favorable to her, and, as for the product of conception, the chances of its viability are rather poor (in adult diabetic women, however, pregnancy is more often carried to its normal conclusion). If the patient is a young man, the conditions in regard to marriage are not much better, in view of the serious character of diabetes in young subjects. In the case of a middle-aged man, with diabetes of mild degree, marriage is, to be sure, possible; but the virility of a diabetic cannot be counted on to any great extent.

TREATMENT.—As in the case of any other disease, before beginning the treatment of diabetes, the patient should be given as complete an examination as possible, in the course of which he should be closely questioned concerning his habits of life. It is often a difficult manner to keep a sufficiently close watch over the patient's doings; consequently it is useful to control their statements by those of persons living with them, points being thus learned which would otherwise have escaped notice.

Information as to the patient's habits and tendencies having been secured, an inquiry into his present condition is made, as well as into his antecedents and past medical history. The urine examination, next carried out, yields knowledge of the specific gravity and acidity of the urine, of its content of sugar and urea, and of the presence or absence of albuminuria and acetonuria. In the event that it contains no or very little albumin, *that it does not give a positive Gerhardt test,* that the patient does not present any organic lesions (tuberculosis, etc.), and that there are no disturbances of nutrition other than the diabetes—in other words, that the diabetes is uncomplicated, whatever be the percentage of sugar present—the treatment will be a relatively simple one.

In such a case there exists, indeed, no fundamental indication other than to reduce the hyperglycemia. This indication should be met in 2 ways: (1) By correcting the cause, if this be possible, and treating the associated nutritional disorders, *e.g.,* gout, etc., and (2) by lowering the hyperglycemia with the aid of a suitable dietary *régime* and of physical and medicinal agents.

A. **Diet.**—The diet is more important than the medicinal treatment. As in all diabetics the power of assimilating sugar is more or less diminished, it is important to limit the ingestion of carbohydrate food. The rule is to forbid it as far as necessary, and to advise a diet of meat, fish, eggs, and green vegetables, particularly those which contain but little starch.

Too great a quantity of meat should be avoided.

Where the patient's weight is above normal, the treatment will, as a rule, prove easy. Indeed, by a reduction cure, recovery from, or at least improvement in, the diabetes can be secured. If the body weight is much below the normal, however, an embarrassing situation may be presented.

In the latter event, if the amount of sugar excreted in the twenty-four hours is considerable, and if the patient does not bear fats well, the difficulty will be particularly great. Above all, it will be necessary to have the patient gain in weight. The carbohydrates should doubtless be reduced, *but under no circumstance should they be completely prohibited:* a certain daily amount, which generally exceeds 80 Gm., is necessary. Otherwise, the patient will be exposed to acetonemia.

> Untoward symptoms in certain diabetics due to the sudden withdrawal of carbohydrates. The writer rigidly excludes carbohydrates from the diet in the outset of the disease, and allows a gradual return to a limited amount of starchy food as glycosuria decreases and as the individual need of the patient demands. He witnessed a case, however, in which pursuance of this plan resulted in unusual and distressing symptoms. In this instance, within twenty-four hours after withdrawal of all starchy and saccharine foods and the administration of a preparation containing sodium bicarbonate, tincture of opium and Fowler's solution, thirst subsided and polyuria was checked; but with the subsidence of these symptoms, headache, nausea and vomiting appeared. Believing the opium to be responsible for this syndrome, it was withdrawn; but to no avail, as cephalalgia persisted to a distressing degree, as did the nausea also. A return to starchy food in the form of bread was advised, upon the supposition that the symptoms were due to the profound and rapid disturbance of nutrition and the sudden checking of polyuria with consequent failure to eliminate the toxic products of a perverted metabolism, before freely eliminated by the urine. The immediate return of a moderate diuresis and coincidental cessation of cephalalgia and vomiting, with the change of regimen, seem to leave no room for doubt that the distressing symptoms were indeed those of self-intoxication from retention. The lesson that the author draws from this experience is that these disturbances—transitory in the present case—might attain a severity which would be disastrous when diabetes is associated with another morbid condition, such as nephritis, fatty degeneration of the heart, arteriosclerosis, etc., and that in such cases a more cautious therapeusis should be instituted. M. Ribas Y. Perdigo (N. Y. Med. Jour. from Revista de Ciencias Medicas de Barcelona, No. 3, 1903).

If the carbohydrates are too restricted it has been found that there is a risk of aggravating the acetonemia, while if they are given too freely the diabetic condition becomes worse, and the glycolytic insufficiency increased. In each case daily analyses should be made to show how the acetonemia and glycosuria stand respectively. **Sodium bicarbonate** may be given in large doses to saturate the diacetic acid and oxybutyric acid in the blood; and to facilitate the elimination of the latter as a sodium salt. Lépine (Progrès méd., May 6, 1911).

Recent researches have shown that among grave cases there are those which are sensitive to albumin and, in these at least, the old method of giving unmeasured quantities of albumin is wrong. It is of special importance that we have learned that in grave cases meat endangers the tolerance. It has also been proved that a certain scarcity of calories is useful; 25 calories per kilogram is sufficient for many diabetics. Hence Rolisch's advice to use the vegetable diet in grave cases which afford these conditions. Another point is that the carbohydrates of plants are slowly absorbed, thus favoring tolerance, and it may be that the intestinal flora is also favorably affected. It must be noted, however, that not every form of vegetable diet is suitable; it must be poor in carbohydrates and rich in fats, and those carbohydrates must be preferred for which the patient has the greatest tolerance. Herman Strauss (Jour. Amer. Med. Assoc., May 10, 1913).

If the urea excreted does not exceed 0.4 Gm. per kilogram of body weight, I make it a rule not to reduce the amount of meat; otherwise, I reduce it gradually, meanwhile increasing the fats,—a procedure which does no harm so long as fats are well digested and do not cause the appearance of acetone in the urine. (The figure just mentioned is, of course, an arbitrary, empiric one. It would be more scientific to establish a ratio of the urea, not to the kilogram of body weight, but to the kilogram of fixed albumin, as does Bouchard. According to this authority, there is present in the normal male subject 150 Gm. of fixed albumin to the kilogram of body weight. In the obese, the ratio of fixed albumin is, of course, less.)

The patients can be kept in good condition for a longer time when they once thoroughly appreciate the necessity for keeping their food down to the ration which will keep their weight stationary. Any excess over this, especially excess of albumin, particularly meat albumin and casein, is directly injurious. The progressive tendency of the diabetes is best counteracted by this means. In mild diabetes he allows only 2 Gm. albumin to the kilo of body weight with interposed periods of only 1.5 Gm., or 1.5 albumin with periods of 1 Gm. In very severe diabetes not more than 1 Gm. albumin should be permitted per kilo of body weight, with interposed periods of only 0.5 Gm. When the patients are on light work, 35 or 40 calories per kilo are sufficient and 45 to 50 calories on heavier work—always provided that the urine is free from sugar or contains but a few grams in the twenty-four hours. With larger amounts of sugar in the urine an allowance must be made for the loss of these calories in the sugar lost. Children must have more calories per kilo than adults. M. Lauritzen (Therap. der Gegenwart, Feb., 1913).

I. Reduction of Carbohydrates.—Reduction of the carbohydrates, as Naunyn says, exerts the advantageous effects not only of lowering, during the time the patient is subjected to it, the proportion of sugar in the body fluids, but also of insuring subsequently, at least in the majority of cases, a higher degree of tolerance for these substances: The relative degree of functional rest allows of the recovery on the part of the organism of a part of its glycolytic activity.

Tabulated metabolic findings in six diabetics on different diets. They show that the conditions in respect to utilization of the diet vary widely in different diabetics; some tolerate and thrive on what others cannot stand; this applies particularly to fat. It is impossible to formulate any general rules applicable to all. Hartelust (Therapie der Gegenwart, March, 1912).

Bread and Starchy Foods.—Many diabetics consume starches to excess, but in the case of most of them it is through the ingestion of bread that the largest amount of carbohydrates is brought into the system. One hundred Gm. of bread contain 53 Gm. of carbohydrates (the best quality breads may contain more than 55 Gm.), which, becoming transformed into glucose, will yield a still larger amount of the latter (about 60 Gm.). Thus a diabetic patient consuming 0.5

kilogram of bread daily can cause, theoretically, to pass into his system more than 260 Gm. of glucose, which is itself more or less refractory to assimilation. In view of this, the importance of greatly restricting the amount of bread ingested can be easily realized.

By virtue of a mistaken idea which is only too prevalent in diabetics, most of these patients imagine they are doing the proper thing if they eat only the crust of bread. It is quite true that the interior portion is generally harder to digest than the crust; but, on the other hand, it is in reality less harmful for a diabetic to eat the inner portion, because, bulk for bulk, it contains a little less carbohydrate material than the crust. Besides, as it is not so appetizing, the patients will not be tempted to exceed the exact amount allowed. This quantity should be as small as possible: I rarely permit a diabetic to take more than 50 Gm. of bread a day; indeed, I often prohibit it altogether, as also those starchy foods,—macaroni or other pastes, rice, sago,—which, in proportion to their nitrogen content, contain more starch than does bread. The table in the opposite column, after Boussingault (Annales de chimie et de physique, 5th series, vol. v) will give a good idea of the relations existing between various foods in this respect.

PERCENTAGE COMPOSITION OF SOME STARCHY FOODS.*

	Proteins.	Fats.	Starch and dextrin.	Water.	Ratio of starch to protein.
Rice	7.5	0.5	76.0	14.6	10.0
Potatoes	2.8	0.2	23.2	73.0	8.3
Sago	9.1	0.6	74.7	13.0	8.2
Vermicelli	9.5	0.3	76.4	12.5	8.0
Bread	7.0	0.2	55.3	36.5	7.9
French cake ("brioche")	10.9	10.9	41.3	17.9	3.7
Gluten preparation	21.3	1.0	64.7	12.2	3.0
Dried peas	23.8	1.6	55.7	13.5	2.3
Lentils	25.0	2.5	55.7	12.5	2.2
White beans	26.9	3.0	48.8	15.0	1.8

*Upon adding together horizontally the figures given in the first four columns it will be observed that the result is not 100. This is because the percentage of the salts has been omitted, and because, in the case of dried peas, lentils, and white beans, the thin covering layer, amounting to from 2 to 3 per cent., is not taken into account.

The last column in this table shows that rice, potato, sago (as well as tapioca), vermicelli (and other similar pastes) contain, in proportion to the amount of nitrogen, more starch than does bread. *A priori,* it would seem necessary that all these articles be prohibited; yet Mossé (Rev. de méd., 1902) has shown that certain diabetics do well when allowed potatoes. Such a diet, which is applicable only to diabetics in whom the glycolytic power is not too greatly reduced, acts in particular by diminishing the intake of animal protein, which is a source of glucose.

> Every diabetic sooner or later requires some starchy food which must be metabolizable to a certain degree and not unduly activate a dormant nor intensify an existing glycosuria, and should exhibit antiacetonemic properties. These characteristics are possessed by the polished rice of commerce. Practically all the rice is absorbed and a certain amount is assimilated by the diabetic, while material rich in cellulose (wheat and oat grits), no matter how much albumin and fat may have been added to it, furnishes little more than a starvation diet. Moreover, pronounced cases of acidosis are frequently cured by the ingestion of 100 Gm. (3.33 ounces) of rice. Stern (Med. Record, June 29, 1912).

Von Noorden, in lieu of potatoes, has advised **oatmeal.** It is given to patients in admixture with a large amount of fat, so that the term "oatmeal cure" is not strictly correct. Blum (Sem. méd., July 5, 1911) says that oatmeal does not act in a specific manner, and that that which lends effectiveness to the treatment is the interpolation of "vegetable days" (*i.e.*, days of insufficient alimentation) and the prohibition of meat. In truth the action of oatmeal is complex. The intestinal flora takes part in this action by apparently causing, when meat is totally excluded from the diet, partial fermentation and oxidation of sugar in the intestine. Von Noorden had already noticed that the oatmeal cure did not succeed when the patient ate meat. Hence the fact that he only gives vegetable albumins with it. In fact, notwithstanding the great notoriety that this cure has enjoyed, it only succeeds exceptionally.

Rye bread is satisfying, stopping the "empty" feeling experienced. Patients eat but little of it in proportion to wheat bread, about a loaf and a half sufficing for a week. It contains but little digestible starch, is laxative, the sugar in the urine diminishes considerably during its use, patients do not tire of it, and it is cheap. Its greatest use is in the milder forms of glycosuria occuring in the middle-aged or old. Lidwill (Intercol. Med. Jour. of Austral, Aug., 1905).

While occasionally the stomach will rebel and refuse to tolerate oatmeal for any great length of time; while the diet is not suited to all cases, being of least avail in the milder forms; while it fails even in some of the severer types, and while no claim for a cure of diabetes can be made, oatmeal still remains a most valued therapeutic agent for the warding off of impending coma in the severer types of diabetes and for assisting in the establishment of a tolerance for carbohydrates. In the milder types of diabetes the writer has so far seen no ill effects follow its use, but the benefits have been trifling. The writer's experience in using it in the diabetes of moderate severity has in general been favorable, it being of especial help in establishing tolerance for carbohydrates. In the diabetes of children, if employed early, it seems to exert a usually favorable influence. J. B. Herrick (Jour. Amer. Med. Assoc., March 14, 1908).

Wheat flour becomes transformed to sugar and the transformation stops there, while oatmeal is transformed a step farther and is assimilated as an aglycogenic, anhepatic carbohydrate, and has thus an antiacetonuric action. M. Klotz (Berl. klin. Woch., Sept. 12, 1913).

Oatmeal diet best method of treating acidosis. In new cases with some toxemia it is the best food to use for a few days, leading the way to other methods. If continued over a week without intermission, however, it tends to cause, especially in children, diarrhea or severe constipation, usually with severe tympanites. Method of employment: Put 11 ounces (330 Gm.) of dry oatmeal in 3 pints (1½ liters) of water, slightly salted, and cook for at least six hours. While still hot, strain through sieve, when, if cooking has been thorough, only coarse covering of kernel will remain on sieve. Finally, add 5 ounces (150 Gm.) of butter and stir in. Patient takes the total amount daily in equal fractions (about 7 ounces—210 Gm.) every two hours, or in larger allowances less frequently. No other food to be permitted except a little black coffee or brandy. Foster (Amer. Jour. Med. Sci., Jan., 1911).

The beneficial effects obtained by the oatmeal diet in diabetes are to be explained mainly by the absence of meat from the diet. The oatmeal cure should always be preceded for a few days by a diet containing a minimum amount of bread—less than 50 Gm. (1⅔ ounces). The oatmeal diet should continue for a period of three or four days and then be followed by one or two green vegetable days. This process is repeated if necessary, but the treatment must not be continued for weeks at a time. This treatment is only necessary for the moderately severe and the severe cases.

Equally good results may be obtained in some individual patients with rye or wheat meal instead of the oatmeal, but oatmeal starch has qualities that makes it superior to other starches for the majority of diabetics. Magnus-Levy (Berl. klin. Woch., Bd. xlviii, S. 1213, 1911).

Von Noorden observed that edema not infrequently resulted during the oatmeal treatment; others have held that it was only observed when bicarbonate of sodium was also being taken. Mirowsky in fact claimed that the oatmeal was the sole cause of the edema. The latter view was found by the writer to be correct, but that edema only occurs when the urine becomes alkaline, and that the rôle played by the oatmeal is in helping the bicarbonate to produce the alkalinity. He found that when the bicarbonate made the urine alkaline without causing edema, the addition of the oatmeal did not alter the case; but that when the bicarbonate failed to change the reaction of the urine, the oatmeal in addition caused edema to appear in some cases together with an alkaline reaction in the urine. Borechardt (Deut. med. Woch., Nu. 37, S. 1761, 1912).

From personal experience the writer can confirm the effectiveness of von Noorden's oatmeal cure in certain cases. In individuals in whom coma was threatening or had already begun, the prescription of an oatmeal cure acted for the moment as virtually life-rescuing. But this happens only in a few cases, and the results are not permanent. O. Minkowski (Med. Record, Feb. 1, 1913).

Little benefit accrues to the patient if attention is fixed upon the glycosuria alone. There is always present an enormous irritability of the *sugar forming apparatus of the liver*. Lack of coordination between the intensity of stimulus and extent of response is the characteristic feature of the disturbed metabolism in diabetes.

In the matter of treatment the excessive irritability of the sugar mechanism must be calmed and every burden avoided. In slight cases a wise choice of food and the exclusion of other irritants will suffice to maintain sugar production within normal limits, and although not cured and liable to get out of order through any indiscretion, the new conditions make for healing or at least a real and persisting improvement, during which nature can effect a cure. Carbohydrates may be given in amounts of 80 to 100 Gm. (2⅔ to 3⅓ ounces) in most cases, protein in lessened quantities, and an increased ration of fats. Alcohol acts as a food and appears to diminish the formation of sugar. The use of opium is limited by its many drawbacks. The value of the mineral water cures is that for a month patients live, eat, and drink rationally, in an environment free from worry and care. Overindulgence in food must always be guarded against. Carl von Noorden (Amer. Jour. Med. Sci., Jan., 1913).

In the French cake known as "brioche" there are 3 or 4 parts of starch to 1 of nitrogen. This article is therefore far superior to bread; it possesses the additional advantage of including a very large proportion of fat.

As for **gluten** preparations, if one relies upon published analyses, there are available some biscuits containing more albumin than carbohydrates, with a rather high proportion of fat. Some diabetics do quite well with these preparations, which would be worth recommending were the expense entailed not so great. Along with them are to be had numerous varieties of bread, daily increasing in their multiplicity in keeping with advances in manufacture.

Soy bean, the seed of *Glycine hispida*, an annual leguminous plant which originally grew in a wild state from Cochin China to the south of Japan and to Java, has been known in the United States for many years, but has been grown chiefly as a forage crop, little attention being paid to its value as a food for man. The bean is peculiar in containing little or no starch, though having a large percentage of protein, which may be utilized in the body in place of that of other vegetables and of meat.

From their experience with this food in 8 diabetic patients, the writers consider it a valuable addition to the dietary. The patients were placed first upon an unlimited diet; second, upon the restricted (usual diabetic) diet; and, third, upon restricted diet, together with the soy bean. In every instance except one, in which the elimination of sugar had already entirely ceased under the ordinary diabetic diet, there was a marked diminution in the percentage and total quantity of sugar passed when the soy bean was included in the dietary.

The bean is palatable and can be prepared in numerous ways. The beans may be taken as a vegetable by soaking them for about twelve to sixteen hours, until the skins come off, stirring until the skins rise to the surface and can be removed, then boiling in salt water or with bacon until soft, and seasoned. When the bean is not available the gruel flour from the soy bean is even more serviceable, containing a greater percentage of protein than is present in the whole beans. The flour can be utilized either as a gruel, in broths or in biscuits or muffins. Inasmuch as the soy flour contains no starch the addition of some wheat flour (1 part to 5 parts of soy flour) in making muffins is required. The proportion of protein to carbohydrates is 8 to 10 times as large in the mixed soy and wheat flour as in gluten flour. In the cases in which this food was used the soy bean replaced largely the gluten of wheat bread, while the patients still remained upon the usual diabetic diet. As it contains no starch, it is exceedingly difficult to make a bread without the introduction of a certain amount of some other flour, but Lecerf, a French pharmacist, is said to have made a bread which resembled somewhat ginger bread, not at all disagreeable to the taste, and which contained no starch whatever or a very small percentage. Lailleux treated a number of cases of diabetes in Algiers with the soy bean with admirable results. J. Friedenwald and J. Ruhräh (Amer. Jour. of Med. Sci., Dec., 1910).

The dry vegetables,—peas, lentils, and white beans,—referred to last in the table on page 51, contain, for each gram of carbohydrate, about four times as much of vegetable albumin as bread. Theoretically, these articles should not be harmful in diabetics, since for 1 Gm. of nitrogen there are supplied but 2 Gm. of starch. It seems to be difficult, however, for an individual with any appetite to content himself with a single spoonful of peas or lentils. If he takes more than this, he will be absorbing a rather large absolute quantity of starch. The question of *bulk* in relation to the various articles of food is of importance in diabetes, for if the patient does not experience the sensation that his stomach is full he will remain quite hungry.

The key-note of the dietetic treatment is not the qualitative but the quantitative restriction of food. It is not sufficient to give the patient a diet list of foods allowed and forbidden, because every case has a different amount of tolerance to carbohydrate and to proteid. There are also those remarkable cases in which the true carbohydrate is tolerated better than that formed in the destruction of proteid, so that while they may be allowed a considerable amount of carbohydrate food without an increase in sugar excretion, they cannot stand any excess of proteid.

The first step in the treatment must therefore be a determination of the tolerance to these two foodstuffs. In practice, we put the patient on a diet containing 100 to 120 Gm. (3⅓ to 4 ounces) proteid, and then we cut down the amount of carbohydrate from day to day. If the patient becomes sugar-free on a simple restriction of carbohydrate, his case will be easy to handle and the prognosis is good.

It is wrong to interdict all carbohydrate food in every case simply because the patient is a diabetic. There is a certain limit of tolerance in every case, and this must be determined at the outset. Schmoll (Calif. State Jour. of Med., May, 1912).

I am rather lenient, therefore, in the matter of watery vegetables, even those looked upon with suspicion by many physicians and patients because of their more or less sweet taste. Thus, I allow squash,—in moderate amounts only, of course. This vegetable, indeed, contains more than 90 per cent. of water and less than 6 per cent. of carbohydrates (the potato contains 20 per cent.). Protein material is itself present in a not inconsiderable amount in squash,—1 part to 6 parts of carbohydrate,—while bread, for every part of protein, contains nearly 8 parts of starch. The difference, it may be suggested, is not very marked, but, in view of the large proportion of water contained in squash, the ingestion of much carbohydrate in eating the latter is unlikely.

It is for this reason, in fact, that green vegetables constitute a very valuable food for diabetics. They are poor, of course, in nitrogen; but they are still more so in carbohydrates, when cooked. Some, *e.g.*, salad, contain no more albumin than carbohydrate, even when uncooked. Moreover, the green vegetables have the advantage of possessing, like fruits, various peptic substances with an agreeable taste.

The success of dietetic treatment of diabetes depends very largely on the skill in cooking which is at the disposal of the patient and particularly on the varieties of appetizing dishes which can be made from foods with the help of the starchless flour and the various sugar-free jams and cakes which are provided. If the patient is on a fixed allowance of carbohydrate it is a good plan to supply him with a list of the various ways with which he can supply that amount. Spriggs (Lancet, Oct. 28, 1911).

Restriction to vegetables once or twice a week is an admirable way to regulate the diet without keeping the patients under constant restrictions. This is useful not only in diabetes and obesity, but also with gout, giving the preference to the purin-free vegetables and fruit and avoiding spinach, peas and beans, as these contain purins. Green vegetables and salads are allowed at will; this amounts to practical starvation without the patient suffering from hunger. He allows as beverage only tea or lemonade with saccharin. In this way the calories can be reduced by a fourth to a half on an average during the week without discomfort to the patient. Disqué (Therap. der Gegenwart, Oct., 1912).

From the same standpoint, *new* potatoes may be assimilated to green vegetables. The starch granules have not yet formed in them, as may be seen upon staining sections with iodine (Faucher, Bull. de la Soc. Méd. des Hôp. de Paris, 1911, p. 738). Hence there is a marked difference between old potatoes and new potatoes. The latter alone should be allowed.

In mild cases of diabetes strict dietaries should be absolutely enforced, as they are then fraught with little danger to the organism. On the other hand, benefit from the treatment is readily attained, there being not only a reduction in the sugar excretion, but even a recovery from diabetes or at least a very considerable augmentation in the tolerance for sugar. W. L. Bierring (Iowa Med. Jour., Feb. 15, 1913).

Fruits.—Fruits are prohibited *en bloc* by nearly all physicians. I believe that this is a mistake, for to be deprived of them is a hardship to many patients. Besides, such a restriction hardly seems justifiable when it is recalled that almost all fruits, even those having a distinctly sweet taste, contain hardly any more carbohydrates than the vegetables which diabetics are allowed. Weight for weight, says Kraus, fruits contain six to twelve times less carbohydrate material than wheat bread. About 200 Gm. of *peeled* oranges are required to furnish an equivalent to the amount of sugar occurring in 20 Gm. of bread.

In apricots the proportion of carbohydrates does not appear to be any greater. In the peach it is even slightly less. This fruit therefore permits of satisfying the whims of diabetics. Even in consuming 100 Gm. they ingest only a negligible quantity of sugar.

It must not be forgotten, moreover, that among the various saccharine substances, estimated all together, and termed "sugar," all is not necessarily harmful to the diabetic. Thus, pentoses, even when not utilized by the body, can in most instances pass through the system without any prejudicial effect; they increase the *glycuria,* but not the *glycosuria.* Other sugars are utilized, if the amount taken is not too great, *e.g.,* levulose.

A few diabetics tolerate lactose fairly well; but it is especially in milk itself that it is availed of. Now, milk is a complex food product, and lactose is not the only principle in milk which might augment the glycosuria. In addition to 50 Gm. of lactose to the liter, milk contains about an equal proportion of casein, which can supply sugar.

Diabetics have been known to assimilate 3 liters of milk and even more, but this is hardly to be observed in any other patients but those kept on an exclusive milk diet. Maurel, of Toulouse, has brought about recovery in diabetics with the "milk cure"; in these cases the milk acted through suppression of excessive alimentation and stimulation. In most cases the tolerance for milk is low. Although when in a strict *régime* the patient has no glycosuria, the latter appears after ingestion of a half-liter of milk. The use of lactose-free milk has therefore been advised. Wright has suggested the following method of preparation: To the milk are added 3 or 4 parts of water acidulated with acetic acid; the casein and fat are thus precipitated. The milk is then filtered through cheesecloth, the precipitate washed and redissolved in a saline solution containing in suitable proportion the salts of the serum.

I have made use of this method of preparation in several cases, but the patients, as a rule, find this artificial milk unpalatable. It may be sweetened with saccharin. Williamson merely dilutes cream with water. Cream as a matter of fact contains almost 4 per cent. of milk-sugar, but, since only a rather small amount of it is mixed with a liter of water, the patient ingests, on the whole, but little sugar. Unfortunately the taste of this mixture of water and cream is hardly, if at all, satisfying. Kefir, which contains no lactose, but a little alcohol and lactic acid, is generally much more readily accepted by the patients.

By correcting the autointoxication, one can remove the irritating influences on the sugar-regulating apparatus. *B.*

bulgaricus (lactic acid bacillus) destroys putrefaction and so overcomes the autointoxication; the bacillus changes the reaction of the intestinal tract from an alkaline to an acid condition; carbohydrate digestion is inhibited or is rather very much slower in the presence of this lactic acid; by thus lengthening the time of carbohydrate digestion only small amounts of sugar are formed and absorbed; permitting only small amounts to be formed and absorbed increased gradually the tolerance for carbohydrates until a normal tolerance is established. While it is agreed that in cases that have come to autopsy there are changes in the pancreas, especially in the islands of Langerhans, and that these changes are probably present in all cases of diabetes, with perhaps irritation and changes in the suprarenals, thyroid, nervous system, and hypophysis, still these changes are also caused by autointoxication. In a series of tests made on starch digestion by pancreatic juice, both that of the dog and man, and carried out for a period of several weeks, the writer found that the digestion of the starch goes on very much slower in the presence of the *B. bulgaricus* than when pancreatic juice alone was used. The bacillus generates free lactic acid, and in order to see whether this bacillus alone or the acid it generates interferes with the digestion, a solution of lactic acid of similar strength to that present in the culture was used with the same result as to the starch digestion. In other words, the Bulgarian bacillus generates the free lactic acid, and it is this acid condition of the bowels that interferes with the rapidity of the starch digestion. Horowitz (Med. Rec., Jan. 25, 1913).

II. **Proteins in the Diet of Diabetics.**—If, in a diabetic patient, the carbohydrates in the diet are greatly cut down, it is evidently necessary, in order to supply with the food the required 2000 to 3000 calories, to increase the proportion of protein substances and fats, and this must be done *with proper judgment,* for in some diabetics an exaggerated intake of proteid food induces a marked increase of the glycosuria. Both experimental research and clinical observation have demonstrated this (Külz, Naunyn, Linossier). Personally, I have also for several years laid stress on the necessity of avoiding the abuse of meat in diabetics. The chief difficulty is to establish a limit, as there are idiosyncrasies.

Nature of Proteins.—The nature of the albumins taken is not without importance. In certain diabetics meat—especially raw meat—produces much sugar, and casein even more than an equal weight of egg albumin. Vegetable albumin is the variety that yields the least sugar. As a general rule, it is believed that the albumins which produce the most sugar are those which are most rapidly absorbed. It is thus necessary, through a process of groping about and exclusion, to select those proteins which conform best to the patient's idiosyncrasies.

III. **Employment of Fats.**—In diabetics *without acetonuria,* free use—not abuse, however—of fatty substances finds hardly any contraindications except obesity and the condition of the digestive tract. These substances are advantageous, since 1 Gm. of fat yields 8.6 calories, while equal amounts by weight of albumin and carbohydrates yield only 3.6 and 3.8, respectively.

Fresh cream, fresh butter, animal fats, and cocoa are generally well borne, even in large amount.

[Cocoa is not an exclusively fatty article. Some brands contain an enormous proportion of carbohydrates,—up to 49 per cent. Diabetics must naturally avoid the latter.

But there are also available cocoas containing only 12 per cent. Butter contains 8.5 per cent. of carbohydrates.]

There are diabetics who will readily take **olive oil**, and even some who, having no distaste for **codliver oil**, are benefited by taking it.

[It is possible, as counseled by Maignon, to administer daily to diabetics 2 or 3 spoonfuls of an emulsion of oil. Rochaix has suggested the following formula:—

℞ *Freshly prepared medicinal soap*	♏xl (2.5 c.c.).
Cherry-laurel water	fʒv (20 c.c.).
Distilled water	f℥iiss (80 c.c.).
Oil of sesame, enough to make	Oj (500 c.c.).

To this may be added some aromatic flavoring agent, or saccharin, if the patient so requests.]

IV. **Alcoholic Beverages.** — There is general agreement as to the necessity for forbidding to diabetics sweet liqueurs; champagne, which may contain over 12 per cent. of sugar; vermouth, which may contain 11 per cent., etc. Beer must also be included among the forbidden beverages, especially certain varieties that contain 5 per cent. of carbohydrates and probably other injurious substances. Cider is also deemed harmful. But ethyl alcohol in moderate amount, diluted with water, or in the form of a good quality of wine, is, on the contrary, useful in these patients, except where there are contraindications arising from the condition of the liver or alimentary tract. It supplies, for each gram of alcohol ingested, about 7 calories; at times favors the digestive functions, and does not increase the glycosuria. Von Noorden has even reported a case in which it reduced the latter. This is, however, exceptional.

V. **Condiments with a Sweet Flavor.**—**Saccharin** is used by diabetics because of its sweet taste. It is employed in the preparation of certain food products intended for their consumption, notably in chocolate. Although its harmful properties have been exaggerated, it is certain that it is capable of causing dyspepsia. Its use may be tolerated, but should not be recommended. **Levulose**, according to S. Solis-Cohen does not increase the excretion of sugar. **Lactose** and **inulin** are also used to replace sugar.

Hediosit, first recommended by Rosenfeld as a substitute for sugar in the dietary of diabetics, has the formula $C_7H_{12}O_7$. It has a sweet, pleasant taste, making it agreeable to take, and is much superior to other substitutes for sugar in that it can be oxidized and be of food value. The glycosuria is not only not increased by the administration of hediosit, but even seems to be diminished by its use. It seems to increase the tolerance of the diabetic for other carbohydrates. With the exception of slight diarrhea when used in large amounts no untoward effects are observed from its administration. It is a distinct addition to the dietary of diabetics and, when given in doses of from 10 to 30 Gm. (2½ drams to 1 ounce) a day, is easily oxidized and utilized in the chemistry of diabetics. Kretschmer (Berl. klin. Woch., Bd. xlix, S. 2221, 1912).

B. **Medicinal Treatment.** — Apart from the diet, remedies are but slightly efficacious in diabetes, but at times they are useful adjuvants to it.

Drugs are of little if any use and as a rule should not be used. When they are not given the patient is made to realize the importance of dietetic and hygienic measures. The amount of food permitted is quite as important as the kind; even non-starchy food must be used in moderation. Each mouthful must be chewed thoroughly; this is one of the most important details of treatment. A mildly **alkaline drinking water** should be used freely; distilled water should be prohibited. Constipation should be overcome with the aid of **castor oil** and **olive oil**; salines and drastic purgatives are to be avoided. A moderate mental laziness combined with moderate physical activity is the ideal for the diabetic. Hodgson (Con. Med. Assoc. Jour., Oct., 1912).

Antipyrin is used in certain cases of diabetes in which the hyperproduction of sugar is very great. My researches have shown that it tends rather to counteract the destruction of the sugar. Its use cannot be long continued.

Salicylate of sodium has also been of service; its action is similar to that of antipyrin, with the exception that it does not equally diminish the polyuria.

Quinine acts in the same way as the antipyrin and the salicylate of sodium, and has the advantage of being tonic.

Opium reduces both the polyuria and the glycosuria, and fulfills certain indications. It is not, however, whatever may have been said on the subject, a really curative remedy. Nonetheless it cannot be denied that it exerts an antiglycogenic action, through the intermediary of the nervous system.

Study of the effects of opium, or its alkaloid codein, on various symptoms of diabetes mellitus, in what respect, if any, the crude drug differed from the alkaloid in action, and whether such effects varied with the dose given. For this purpose a series of 9 cases of ordinary diabetes were placed, so far as possible, under similar conditions. **Codein** was given in 7 cases, always in the form of a pill. As a rule, the initial dose was ¼ grain (0.016 Gm.) thrice daily, which was gradually increased, at varying intervals, by ¼ grain (0.016 Gm.) to the dose, or by larger amounts, until as much as 12 grains (0.77 Gm.) was being taken daily. On the whole, the definite results obtained in these cases are disappointing. Possibly the doses given were altogether too small. This does not seem an adequate explanation, however, as in more than one case the results have appeared to become less favorable with increased doses. On the other hand, in a certain small number of cases the effects of gradually increased doses have been favorable even over several weeks. It may be said that inasmuch as codein will quickly lose its first sedative effect, it can only be of value for a short period.

Opium, either in the form of pilula opii or of pilula saponis comp., was given in 6 cases. In 3 of these it was tried before any other drug, while in 3 other cases it was given to patients who had previously taken codein, in order that the effects of the two alkaloids might be compared in the same individuals. The initial dose given varied from ⅕ to 1 grain (0.013 to 0.065 Gm.), thrice daily, and was usually increased gradually. In 1 case up to 12 grains (0.77 Gm.) daily. In spite of the fact that one of the patients became worse and died while under treatment by opium, the general results obtained with it were, on the whole, rather more uniformly successful than those obtained with codein. In 3 cases codein had previously been tried, and comparing the results one sees that opium began to act effectively when codein in increasing doses had ceased to do so. A. J. Hall (Quarterly Jour. of Med., July, 1909).

Opium should be used only in the rare nervous cases or where all else has failed. Dose, 0.03 Gm. (1½ grains) *t. i. d.,* gradually increased to 0.5 Gm. (7½ grains) for from one to three weeks. Disadvantages: The effect is temporary, does not establish sugar tolerance, and may lead to habit. **Bromides** or **antipyrin** can generally be substituted for opium, even for nervous symptoms. **Arsenic** is ordinarily preferable. Given as **Fowler's**

> **solution** in ascending doses until mild toxic effects appear, then gradually reduced. It is especially indicated in severe cases, combined with diet; it is very helpful in neurotic debilitated subjects, but it does not increase sugar tolerance. Its effects are less evanescent than with opium. **Hexamethylenamine,** 5 grains (0.3 Gm.) three or four times a day, reduces the glycosuria and increases tolerance for sugar, but it should not be used in severe cases without proper diet. Forchheimer (Amer. Jour. Med. Sci., Feb., 1911).
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> Having used codeine sulphate for a number of years, and then morphine in gradually increasing doses, the writer has come to the belief that the dried extract of **opium** gives the best results, this being started in half-grain (0.032 Gm.) doses, three times a day, and gradually increased until 4 to 6 grains (0.26 to 0.39 Gm.) daily are taken.
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> The next drug of efficiency, recently so highly recommended by Floerscheimer, is **arsenic.** There is no doubt that practically there are patients who do better on arsenic than on opium, or any other medicinal treatment. **Fowler's solution** commencing with 3 minims (0.18 c.c.) and gradually increasing up to 10 (0.6 c.c.), three times daily, is the most convenient and answers for all purposes. It is well here to remember that while large doses of opium may be employed, with the use of arsenic the doses should always remain small or moderate, for cases not benefited by these doses would only be made worse by larger ones. Anthony Bassler (N. Y. Med. Jour., Oct. 12, 1912).
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> The writer has obtained good results from the following combination:—
>
> ℞ *Extract of valerian,*
> *Pure phenol,*
> of each.... 2 grains (0.13 Gm.).
> *Codeine* ..... ⅓ to 1 grain
> (0.02 to 0.06 Gm.).
> *Extract of*
> *cascara* .... 1½ grains (0.09 Gm.).
>
> The valerian steadies the nervous system, the phenol disinfects the intestinal canal, the codeine controls the output of sugar, and the cascara provides for the daily evacuation of the bowel. Rankin (Brit. Med. Jour., March 22, 1913).

In a few cases **belladonna**—or **atropine**—combined or not with opium, have seemed useful.

> **Atropine methylbromide,** 2/15 grain (0.009 Gm.) *t. i. d.,* gradually increasing to 8/15 grain (0.034 Gm.), or **atropine sulphate,** 1/150 grain (0.0004 Gm.), gradually increased to 1/20 grain (0.0032 Gm.), are well adapted to milder cases. The glycosuria is often diminished and the carbohydrate tolerance increased. The tincture of belladonna seemed best tolerated. Sodium bicarbonate, in quantities sufficient to make urine neutral or slightly alkaline, is indicated when large amounts of acetone or ammonia occur in urine. Certain carbohydrates, *e.g.,* oatmeal and potatoes should be used, but a milk diet is better in some. Forchheimer (Amer. Jour. Med. Sci., Feb., 1911).
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> All medicinal substances thus far employed in the various forms of diabetes are, at the best, only symptomatic remedies. Rudisch advocates the use of atropine sulphate and atropine methylbromide in diabetes. The writer tried atropine methylbromide in about one dozen cases of moderately severe and grave cases of diabetes—in more cases he did not dare to. In all there ensued more or less pronounced atropine poisoning; in two cases of the moderately severe type the glycosuria disappeared after a few weeks' dieting and the administration of atropine, an increased tolerance for carbohydrates was not noted in these cases thereafter; in none of the remaining instances, which were nearly all of the grave type, did the atropine produce any other effects than those of a toxic nature. Stern (Med. Record, July 22, 1911).

Bromides in certain cases, especially in nervous diabetes, would seem *a priori* capable of reducing glycogenesis. In reality, however, they are of but little utility, and their depressing action prevents their being administered indefinitely.

Alkalies, on the contrary, are useful, in moderate doses, in nearly all diabetics and for a prolonged period. They are known to favor oxidative processes (probably by becoming transformed into peroxides). It seems likely that they act in this way in diabetes. It is possible, however, that their effect is not limited to the favoring of oxidation, but that they contribute to the fixation of glycogen in the liver, that is, to what I have termed "euzoamylia." In certain cases, they increase glycogenesis and glycosuria; these are generally diabetics in a poor state of nutrition.

The salts of **manganese** form an integral part of the oxidases (Bertrand). But the oxidases have no action upon *glycolysis*. This implies that manganese cannot much be counted on for curative properties in diabetes.

> The writers have cured or have greatly improved a number of cases of diabetes by means of inhalations of **ozone** given in daily *séances* of fifteen minutes each. It is supposed that oxygen in the naissant condition reestablishes the equilibrium between the production and the consumption of sugar in the tissues. D. Labbé and P. Perochon (Presse médicale, March 22, 1913).

Jambul, a plant of the order Myrtaceæ, possesses only a very feeble antiglycogenic action.

Hepatic opotherapy has been recommended by Gilbert and Carnot in cases where the functional activity of the liver-cell is distinctly diminished. Sometimes it has given good results in these cases.

It is known that the internal secretion of the pancreas, in addition to its property of exciting glycolysis, possesses that of contributing to the fixation of glycogen (euzoamylia). Theoretically, it was justifiable, therefore, to expect a good deal from **pancreatic opotherapy**. As a matter of fact, the results have almost always been disappointing, which shows that we are as yet unable to prepare an extract of the pancreas that is equivalent to its internal secretion.

> Deficiency in one or more ferment actions plays an important rôle in the causation of diabetes. He has used tablets containing various ferments, including those of the **pancreatic secretion**, in a series of cases, with the result that glycosuria was almost or quite removed. Schnée (Zentralbl. f, innere Med., Aug. 10, 1912).

[Transplantation of the pancreas of an animal under the skin of a diabetic would only be justifiable (in cases where pancreatic insufficiency is with certainty known to exist) were the chances very good that a transplanted pancreas would preserve its functional activity. In the present state of science, however, there is ground for believing the contrary. Finally, the fact should not be lost sight of that the operation, even if most carefully conducted, may be followed by local infection and suppuration. R. Lépine.]

C. **Physical Agencies. — Physical exercise**, so wisely recommended by Trousseau and Bouchardat, who considered it an important factor in the treatment of diabetes, may be given first rank among the physical therapeutic measures. Unfortunately, it cannot be advised to all patients, and must even be prohibited in patients that have reached the stage of impoverished nutrition, for fatigue increases the latter. Thus, overstrenuous physical exercise acts in the same manner as mental strain, worry, etc.

Climate.—The value of a winter sojourn in a warm climate does not appear to me to have been sufficiently appreciated in the treatment of diabetes. The underlying principle is not that all diabetics are sensitive to cold, but that the results of rather exact observations seem to have shown that their glycosuria, all other conditions being equal, is less if they stay in a warm climate. This may be due both to the fact that the activity of glycolysis is augmented and that the system is not excited through the influence of the cold to an increase in carbohydrate metabolism.

Electricity.—The galvanic current, static electricity, and more recently the high-frequency currents have been applied to the treatment of diabetes. The results have not been very satisfactory, and even in some cases unfavorable. Thus, De Renzi and Reale, in diabetics from whose urine sugar had disappeared, observed its reappearance after the use of the high-frequency currents.

Radiotherapy. — Our experiments on living dogs and on organs *in vitro* have shown that the X-rays in small doses stimulate glycolysis and that in large doses they restrain glycogenesis. (See Lépine and Boulud: C.-r. de l'Acad. des Sci., Jan. 11, 1904, and Lépine: Treatment of Nutritional Disorders, p. 552, in the volume "Médications générales" of Gilbert and Carnot's "System of Therapeutics.") Theoretically the rays should be of value in the treatment of diabetes; it must be admitted, however, that so far the results obtained have not been favorable.

Treatment of Diabetes with Acetonemia.—As soon as, in a diabetic, diaceturia is recognized — through Gerhardt's test—the principal indication is to bring about cessation of this symptom. Now, in order to accomplish this it is necessary to have a clear idea of its origin.

We have already seen that the normal subject becomes acetonemic after two or three days of fasting or, simply, of subsistence on a diet of meat and fats from which carbohydrates are excluded. The process occurring in the diabetic patient is essentially the same. When he becomes acetonemic, this is because there is not taking place in his system a sufficient consumption of carbohydrates *in relation to* the consumption of proteid and fatty substances. To remedy this condition several means are available.

First of all, in the event that the diet previously imposed had been severe, the patient should be allowed to ingest daily at least 100 Gm. (3⅓ ounces) of carbohydrates. In other words, **partial restoration of carbohydrates is in order.** The glycosuria will be increased thereby, but when the acetonuria shall have ceased the glycosuria may be restrained by again reducing the carbohydrates.

In other cases, on the other hand, it will be necessary to **restrict the** amount of **carbohydrates** taken. This applies to those patients in whom the carbohydrates had not been in too small an amount in the diet, and where the acetonemia was the result of deficient glycolysis. Now, one of the best methods of increasing glycolysis is to limit the amount of glycolyzable material supplied to the economy.

Thus, it will be observed that either one of two diametrically opposed methods, one consisting of a diet richer in carbohydrates, the other involving restriction of them, may, according to the nature of the case, represent the method suitable for correcting the acetonemia.

In certain acetonemic cases, it is the protein (or the fatty) constituents of the diet which must be restricted, for in them an excess of these classes of foodstuffs has been responsible for the harm. In these cases acetonemia will be overcome by **restricting the intake of fats.** Sometimes it is not an excess of fats in general, but one particular sort of fat, which is prejudicial. Finally, in still other cases it is certain proteid substances that are harmful. Indeed, there are sometimes idiosyncrasies in this direction, the nature of which can be recognized through process of exclusion. In a general way, butter yields to the body more fat than other fatty substances.

From all this it will be gathered that in the presence of a diabetic not in a condition of acetonemia a diet poor in carbohydrates must be prescribed, while in an acetonemic case no fixed rule can be followed, empiricism being the guide in establishing the diet.

> The acetonuria which occurs in diabetic patients who are subsisting upon a diet of proteid and fat, and who are getting no carbohydrates, is due to the presence of the fatty elements of their regimen. The healthy individual, when put upon a diet of fat and proteid only, exhibits an increased elimination of acetone, and this augmentation is more marked in the diabetic. To obviate the difficulty the author suggests that **alcohol** be substituted for the fat. The quantity should be about 10 drams (2½ Gm.) daily in the form of wine, beer, tea *au rhum,* etc. The diabetic patient bears the alcohol well and it is likely to cause neither excitation nor depression. Romme (Presse méd., No. 89, p. 712, 1906).
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> The daily amount of acetone bodies excreted in the urine gives a measure of the severity of the disease. The administration of alkalies can markedly increase the excretion of the acetone bodies without any increase in the formation of these bodies, and consequently without any added danger to the patient. Furthermore, the harmful effects of the acetone bodies is dependent upon the duration of the acidosis. Thus, an acidosis of a mild degree, but long continued, is more to be feared than a higher acidosis of short duration. The acidosis that persists when a patient remains sugar-free on a strict meat and fat diet is harmless. Therefore, it is not necessary to change the strict diet so long as the patient remains sugar-free. However, if such a patient excretes sugar, a daily quantitative estimation of the acidosis is necessary for a rational treatment. The writer obtained good effects of the **oatmeal** in severe cases of diabetes with acidosis. Tüthje (Therap. der Gegenwart, Bd. li, Nu. 8, 1910).
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> In diabetics with denutrition and acidosis the indications are to combat (1) the hyperglycemia, (2) the loss of nitrogen, and (3) the acid intoxication. For the first the intake of carbohydrates should be restricted; for the second, the diet should be rich in nitrogen, and for the third indication the diet should be poor in meat and rich in carbohydrates. These antagonistic indications are best met by **varying the diet** to fit the predominating symptoms at the time. As a rule, the aim is to keep the hyperglycemia within toleration, but when acidosis menaces a **vegetable diet** should be promptly instituted. It is a good plan to allow a week of mixed diet; then three days' restriction to milk; then a week of mixed diet; then three days of oatmeal; then a week of mixed diet; then three days of soft mashed vegetables, etc. In other words **alternate diets** are indicated. Labbé and Bitl (Arch. des Mal. de l'App. Digestif., Jan., 1913).

Medicinal Treatment.—As to this, no uncertainty is possible: alkalies in large doses must be administered. The best guide to follow in this respect is the reaction of the urine. As long as the urine remains acid sodium bicarbonate should be continued in sufficient amount to bring the urine to a *low degree* of acidity, and it will often be a source of surprise to observe what enormous doses of the drug are required to attain this end. It is borne in mind, indeed, that, even if the urine is rendered but feebly acid, acetonemia is not thereby abolished, for the possibility of neutralizing the organic acids does not imply that their production is arrested. At least, a chance is afforded of eliminating their harmful effects.

Where acetonemia has been of long standing, it may be impossible to arrest its progress, even by rational dieting and the administration of large doses of sodium bicarbonate. Such cases, however, are rare, and I have only very occasionally seen an acetonemia that was completely refractory to appropriate treatment. More commonly, unsuccessful results are due to insubordination on the part of the patient himself, to deviations from the prescribed diet, etc., which lead to aggravation of his condition and threatened coma. Under such circumstances what is to be done?

If the administration of sodium bicarbonate by the mouth has proven ineffectual, the injection of this drug into a vein must be considered without delay.

According to personal observations based on more than 10 cases, the best chances are thus afforded of preventing the appearance of coma. When coma exists, an intravenous injection has but little chance of proving efficient. At most, one may succeed by its administration in bringing the patient back to consciousness for a short time,—sometimes a very important result, if the patient is to make known his ultimate wishes. On the whole, I must repeat, when the patient is already comatose, there are but slight chances of success. That this is so will occasion no surprise when it is recalled that the toxic principles inducing coma simultaneously bring about lesions of the nerve-cells in the brain which soon become irremediable.

The situation is a much better one if the injection is administered before the onset of coma, and a single intravenous alkaline injection, by virtue of the sudden alteration in the conditions it produces, will act much more favorably than a slow introduction of alkalies by the intestinal route. In order that the latter shall actually meet the toxic substances, which occur *in the interior of the cells,* it will readily be seen that a sudden change in the *osmotic equilibrium* will be of value.

This change is often followed by the elimination of an enormous amount of the acetone bodies. It would seem as though a flushing of the tissues with fluid were taking place. The alkaline injection thus constitutes a most active form of *symptomatic* treatment.

Following are a few practical details in this connection: I have prepared a solution of 18 Gm. (4½ drams) of sodium bicarbonate to the liter (quart) of ordinary water. This is boiled, then filtered. A vein is then exposed at the bend of the elbow, a sterile glass cannula fastened into it with thread, and the solution introduced at 36° C. (96.8° F.) under a low pressure and very slowly. I have caused to enter as much as 1800 c.c. (3¾ pints) of the solution. In this event the introduction of the fluid occupies a period of one hour and a half. Meanwhile, the pulse is watched and the heart auscultated; if gallop rhythm should be heard, this would indicate that the right heart was being overloaded. The entrance of the fluid should then be temporarily stopped. As already stated, the solution should be 1.8 per cent. strength; it is thus isotonic. A hypertonic solution is dangerous, and a hypotonic one involves the risk of dissolving the red corpuscles.

The intravenous injection is followed by a reaction (afebrile), which is, in general, favorable. I have observed to cease, through the effect of this reaction, progressive acetonemia which alkalies administered by the mouth had not succeeded in overcoming.

Alkaline salts having anions capable of combustion, such as sodium citrate, are in some ways preferable to sodium bicarbonate itself. **Sodium citrate** is advantageous in that its taste allows of its being given with the food or in lemonade. It does not remove the appetite or disturb gastric functions. The author has given amounts up to 50 Gm. (1⅔ ounces) a day without unpleasant consequences. In one case, for example, 20 Gm. (5 drams) a day of sodium bicarbonate caused diarrhea; on replacing it by 30 Gm. (1 ounce) of the citrate, the intestinal disturbance ceased, though the therapeutic effect was as satisfactory as before.

In cases of diabetic coma, sodium citrate might be given intravenously, a method for which the bicarbonate is not suited owing to its greater alkalinity. The feeble alkalinity of the citrate may be entirely counteracted by the addition of a small quantity of citric acid, giving a neutral solution. L. Lichtwitz (Therap. Monats., Feb., 1911).

Treatment of Gangrene. — Dry gangrene in diabetes should be treated like the senile form of gangrene, *i.e.*, preferably by expectancy and **antiseptic dressings.** As for moist gangrene, my experiences with it have shown me that the only rational plan of treatment is to **amputate** through the healthy tissues. It is impossible to act too early in this condition. The patient's safety depends upon prompt intervention. **Chloroform** should be employed as little as possible.

The indications for **surgical intervention** in diabetics do not differ essentially from those in persons not affected by this disease. This statement applies particularly to surgical procedures in cases of mild diabetes, in which, if feasible, the operation can be delayed until the urine is free from sugar. If, however, this is not advisable, as in appendicitis or severe injuries, intervention can be resorted to at once. As a rule, the gangrene of diabetics is not due to the disease, but to the co-existent arteriosclerotic process. When arteriosclerosis is present, the diabetic disturbances of metabolism, even if the glycosuria is of moderate degree, are apt to increase, but recede after the removal of the gangrenous area. As a rule, an arteriosclerotic gangrenous process cannot be arrested by internal treatment. If gangrene is associated with phlegmonous or general infection, it is best not to wait too long for the line of demarcation. Incision should be avoided in furunculosis associated with mild diabetes, better results being obtainable by reducing the amount of sugar in the urine, by **moist applications,** or, later, by **Bier's hyperemia.** Comparatively slight trauma may cause great damage in severe diabetes. If in cases of this kind with acidosis surgical intervention cannot be delayed until the metabolism has been improved, it is advisable to administer **alkalies** by mouth and rectum and to give opium.

If possible general narcosis should be replaced by local anesthesia, but if the latter is not adequate, **ether-oxygen anesthesia**, if necessary with the addition of a little **chloroform**, is indicated. It is always advantageous to determine exactly the character of the diabetes in the individual case and to ascertain whether any existing acidosis is peculiar to the condition or has been exaggerated by the surgical complication. Umber (Deut. med. Woch., Nu. 30, 1912).

If the patient is too weak to bear amputation and if the gangrene, though wet, is not spreading rapidly, it is sometimes possible to inhibit it by use of douches of very **hot**, but **dry, air** (300° C.—572° F., according to Dieulafoy: Bulletin de l'académie de médecine, 19 févr., 1910). These douches, which are not as painful as one would expect, are to be repeated twice a day. In Dieulafoy's case the result was marvelous; the gangrenous tissues became mummified, the ichorous secretion was completely arrested, and the general state of the patient improved. It then became possible to amputate the limb under safe conditions, and recovery ensued.

The writers have called attention to a new method of treatment of diabetic gangrene—the application of air at a high temperature and pressure. They used an apparatus invented by M. Prat, which consists of a source of compressed air and of a generator of heat formed by pieces of platinum, which are made incandescent by a current of carburetted air. By an ingenious device the intensity of the heat and the pressure of the air can be varied as desired by the operator. This method of using **hot air** differs from all previous ones, for a pressure exceeding 15 kilograms and temperatures exceeding 600° C. can be attained, which not only produce active congestion, but sterilization, destruction, and even removal of the diseased tissue. The apparatus of M. Prat was first used on animals in the veterinary school of Lyons in 1889. It is capable of being put to many therapeutic uses, but in the present communication only the effects produced in diabetic gangrene are considered. The gangrenous part is cauterized and deeply roasted by a current of air at a temperature exceeding 300° C. (572° F.). Further, with a current of air at a temperature of 150° to 220° C. (302° to 392° F.) active congestion and slight burns of the living tissues are produced. Sometimes the application is very painful and necessitates administration of **chloroform**, but usually the patient feels little. Often there is such thermo-anesthesia that no pain is felt after large burns of the second degree. Moist dressings of hot sterilized water, frequently renewed, immediately relieve any pain produced. The hot air has several actions on the tissues; it sterilizes, dries up raw surfaces, and deodorizes them. An interesting fact is that the scars which follow the burns produced are perfectly supple and flat, like those produced by radium. Marat and Vignat (Soc. Méd. des Hôpitaux of Paris, April 3, 1908).

The writer obtained striking benefit from the prolonged **inhalation of oxygen**, in several cases in which it very considerably prolonged life and afforded great comfort. One patient, who was evidently not far from an atattack of coma, improved markedly and survived an amputation. In this case for some reason the oxygen was stopped by the writer's house surgeon, and there was an almost immediate change for the worse, and the patient seemed as though death was imminent, but a return to the oxygen brought him out of danger and he was ultimately discharged from the hospital. Lockwood (Lancet, Feb. 10, 1912).

The high mortality resulting from the usual former practice of high amputation in diabetic gangrene, caused the writer to study conservative methods in the treatment of this condition. Its essential features are, he says, defective nutrition due to obliterating endarteritis of the large vessels of the limb with an excessive susceptibility to local death from the perverted metabolism and the greater liability to bacterial invasion, together with the systemic complications of the disease. Amputation is not necessary in the incipiency of the gangrene, and when it does become so on account of the extension of the disease a high amputation is by no means always indicated. He has evolved a method of conservative therapy based on the three following principles: "1. Systemic treatment of the diabetes and prophylaxis against the development of dangerous complications, especially coma. 2. An attempt to improve the circulation in the extremity. 3. The treatment of the local infection on rational general surgical and aseptic principles." Seventeen cases treated by this method during the past two and a half years are reported and analyzed: eleven of the patients were cured; five died and one is reported not improved. The average duration of treatment was two and three-fourth months. The causes of death in the fatal cases were pneumonia, sepsis and diabetic coma, either one of these alone or coma following the two others. Of the 11 patients who recovered, the routine treatment included in 9 cases either no operative procedure at all, or such minor operations as opening an abscess or removal of a gangrenous toe. In the other two, on account of a rapidly advancing gangrene, amputation of the leg at the junction of the upper and middle thirds had to be performed. Each of these patients has a useful stump and a movable knee. While the number is not sufficient from which to draw a broad general conclusion, he says that they were not selected cases and some of them were very severe and all of them would probably have been subjected to amputation under the former methods of treatment. The routine conservative treatment consisted of an antidiabetic regimen guided by daily examinations of the twenty-four-hour urine, the diet being relaxed only when coma impended. The writer has no great faith in any drugs, but he regularly administered **sodium bicarbonate** in large doses (not, however, sufficiently large to derange the stomach), and **codeine** and **morphine** to relieve pain. If anesthesia is required for operation chloroform should never be employed and ether should be used seldom if ever, **nitrous oxide** or **nitrous-oxid-oxygen anesthesia** being chosen instead. The attempt to improve the circulation of the extremities narrows itself down to the production of **hyperemia** by **Bier's** method, which he is convinced is of positive value. Passive hyperemia is contraindicated. On general principles the writer administers **sodium** or **potassium iodide** for their absorbent qualities and **nitroglycerin** as an arterial dilator. Definite directions are given as to local infection. There should be the strictest asepsis and the greatest attention to the needs of the individual case; antiseptics should be avoided as devitalizing, as well as tight bandaging, and retention of pus must not be permitted to occur. As regards **amputation** when required, he never uses an Esmarch bandage and the operation should be done as simply and rapidly as possible and with a minimum amount of traumatism. The suggestion has been made to him by Dr. Garbat that **autogenous vaccine** might hasten the separation of sloughs. The flaps should be relieved as far as possible from all tension and the dressings loosely applied. A word is given as regards prophylaxis; chiropodists should be avoided as well as tight shoes. Many patients date the origin of their gangrene to the clumsy manipulations of a pedicure. DeWitt Stetten (Jour. Amer. Med. Assoc., April 12, 1913).

From a review of opinions of various well-known surgeons, and from limited personal observations, A. L. Fisk holds that the presence of glycosuria in those individuals who may have surgical diseases does not in itself constitute an absolute contra-indication to any and all surgical relief. Very great judgment must be exercised, however, in the selection of cases, in the determination of the kind and extent of the operation to be performed, while the strictest surgical asepsis must be rigidly observed throughout. Infection, when it occurs, is from without, and is the result of an error in the technique. When infection does not occur, the operative wounds heal kindly, but slowly, especially in granulating wounds. The vascularity of the tissue must be interfered with as little as possible. This is particularly so in gangrene of the extremities, in which the statistics of Heidenheim, Kuster, and Smith and Durham show most conclusively the necessity of high amputations.

> Referring to the cases reported by Miller and Joslin of the disappearance of diabetes after extirpation of tumors of the uterus, the writer reports two similar cases in which the glycosuria disappeared after prostatectomy. In one of the cases the disappearance was temporary, but in the other recovery seems to have been complete. The most plausible explanation, according to the author, is that the operation removes some nervous or toxic irritant which in some way, at present unknown, disturbs the carbohydrate metabolism. Of more importance than the theories of causation are the practical points involved. Surgeons have always dreaded operations in severe cases of diabetes, but these four cases would indicate that the prognosis from the operative point of view is far better than is supposed. When diacetic acid or oxybutyric acid tests are negative there is no danger, no matter how intense the acetone reactions may be. If positive the prognosis should be more guarded. M. Manges (Jour. Amer. Med. Assoc., March 1, 1913).

Carbuncles and Furuncles.—These complications are not infrequently met with in diabetes. They should be treated by the methods in use for similar disorders in non-diabetic patients.

> **Passive congestion** or suction therapy tried in a large number of cases of furuncles or carbuncles in diabetics. The writer reports the details of 5 severe cases to illustrate the benefits derived and to urge the more frequent use of the treatment. Grube (Münch. med. Woch., Bd. liii, Nu. 29, 1906).
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> Boils in diabetics, when taken early, may often be aborted by rubbing in a 2 per cent. ointment of the **yellow oxide of mercury** in lanolin. Where they persist, **tonics, vaccine, antiseptics, free drainage,** and sometimes **excision** are valuable. After healing, bathing of parts several times daily for two weeks with an antiseptic solution may prevent further infection of the area. In carbuncles in cases where tissues show but slight resistance, early and thorough removal gives best results. King (Monthly Cyclo. and Med. Bull., Aug., 1911).
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> The author frequently uses **sodium perborate** as a dressing in infected wounds and acute and chronic ulcers. He has also employed it with success to arrest hemorrhage in epistaxis or after adenoid operations and tonsillotomies. He now reports 3 cases of diabetic gangrenous ulcers in which the drug, applied as a powder, rapidly brought about healing,—in one instance after other local medication had failed. The powder was usually applied twice daily. A. Herzfeld (Jour. Amer. Med. Assoc., Nov. 11, 1911).
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> The carbuncle of diabetes mellitus, of all carbuncles, should never be operated upon by excision. Diabetic coma is always imminent. Far better is it to cure this infection of the skin by means of precipitated **sulphur,** applied as a powder into the points of suppuration, or ulceration, or used as an ointment with a cacao-butter base (1 to 8). Equally efficacious to render a carbuncle innocuous is the constant application of a compress wet with a solution of **calcium creosote.** Kolipinski (Monthly Cyclo. and Med. Bull., Aug., 1912).

Conclusions in Regard to Treatment.—To summarize: Diabetes without acetonemia must be treated *medically*, taking duly into account the conditions that gave rise to it and instituting a **diet** capable of diminishing the hyperglycemia. In the presence of diabetes with pronounced acetonemia, it is the latter which becomes the principal indication in the treatment; by groping about, *i.e.*, proceeding in an empiric manner, it is necessary to find the means not only of arresting its progress, but of overcoming it. The plan of diet to be advised in order to attain this end has been set forth above. Simultaneously, the condition should be treated symptomatically with **sodium bicarbonate**, given in as high a dosage as is necessary. However carefully acetonemia be treated, the results of my observations have shown that in a certain proportion of cases (3 to 5 per cent.) it terminates in coma, unless, by means of an *early* intravenous alkaline injection, one is successful in modifying the nutritional disturbance which is keeping up the acetonemia.

(For various features not gone into in sufficient detail in the foregoing study, consult: R. Lépine: "Le Diabète sucré," Paris, 1909.)

R. Lépine,
Lyons.

DIACETYL MORPHINE. See Opium: Heroin.

DIARRHEAL DISEASES OF INFANTS.—DEFINITION.—In itself diarrhea can be regarded as a symptom only, but it has long been customary and is still convenient to group under this name, used generally, all those disorders in infancy which have as their chief symptom an increased motor and secretory activity of the intestinal tract. Such increased activity may, in a few instances, be the result of nervous impulses reflected through the central nervous system, but in the great majority of cases it is occasioned by the presence of irritating material of a more or less noxious character in the canal. In many instances it must be regarded as one symptom only of a systemic intoxication arising from the absorption of the toxic products of pathogenic micro-organisms developed in the alimentary tract; a symptom important in itself, but not to be considered apart from other symptoms of systemic disturbance, such as fever, quickened and enfeebled cardiac action, and nervous prostration.

In some instances, diarrhea must be regarded as a symptom of Finklestein's "Food Intoxication" a disturbance of metabolism due to the ingestion of sugar and fat in larger amounts than the infant's digestive tract can manage.

Inflammatory changes more or less extensive in character develop with varying promptness in the intestinal mucous membrane, in all the more severe diarrheas the result in some measure of the irritating character of the intestinal contents, but in a much greater degree due to a specific action of the bacterial toxins. Not infrequently the bacteria themselves penetrate the tissues of the intestinal wall, inducing destructive changes, aggravating the symptoms, and indefinitely retarding recovery.

All diarrheas involve some impairment of general nutrition; in severe or prolonged attacks the emaciation may become extreme.

Infants under the age of 30 months are peculiarly prone to diarrheal disorders; the mortality in New York City of infants under 2 years, from diarrheal diseases alone, exceeds the total number of all deaths from the infectious diseases of childhood (Holt). In them, to a much greater extent than in older children or in adults, has the disease a tendency to run a severe course, and to terminate fatally. For this reason the etiology and treatment of these disorders demand careful consideration.

ETIOLOGY.—If we inquire into the causes which induce this special liability to diarrheal disease on the part of infants a few facts stand out prominently.

The Season.—Diarrhea takes a comparatively unimportant rank among infantile disorders during the cooler months of the year. With the onset of warm weather, however, diarrhea suddenly acquires importance, owing to the frequency with which it is encountered, to its severity, and to its large mortality. This is evidenced by the statistics of all large cities in the temperate zones. Whenever the minimum temperature of the atmosphere for the twenty-four hours reaches the neighborhood of 60° F., diarrheal disorders assume the character of a widespread epidemic, an epidemic which reaches its height during the months of June, July, and August, and gradually subsides with the oncoming of cooler weather. Unquestionably the depressing effect of high temperatures upon the nervous and especially upon the vasomotor system of the infant plays an important part in the etiology of these disorders. Much more important, however, is the effect of continued heat on the development of bacteria in food materials which may be used for feeding the infant and especially in cows' milk; of this we speak later on.

There is a winter diarrhea of children strongly resembling the summer diarrhea. In one case the diarrhea was found to result from the freezing of milk, which spoiled it, and caused curds to form on thawing. After straining the milk the diarrhea disappeared. The diarrhea of frozen milk is not so severe or debilitating as that of the summer season. If need be, the child can be taken off the milk diet for twenty-four hours and given barley water in the interim. Shelmerdine (N. Y. Med. Jour., March 14, 1908).

The influence of a tropical climate on children is shown most decidedly in Cuba by the frequency of gastrointestinal disturbances even more than by the mortality. The long persistence of the heat is responsible for their development both in adults and children, and the children seem to be born with a predisposition for various gastrointestinal disturbances. At Havana are encountered all forms of digestive affections known and described by the classic writers of all countries. Duenas (Bull. de la Soc. de Péd., Nov., 1910).

Hitherto attention has been devoted too exclusively to the infant's food while the infant itself has been disregarded in our study of infantile mortality. The author has found the mortality highest in the cities and in the hottest parts and in the hottest houses and rooms, and he has become convinced that the heat is an extremely important factor. It debilitates the children so that they feel any slight digestive disturbance far more severely and succumb more readily. The campaign against infant mortality is thus seen to be essentially a housing problem. Until the population began to accumulate in the cities, an excessive summer mortality among infants was known in Germany only from the reports in American literature, so that cholera infantum was long called the "Amercan disease." Not until about 1870 did it attract attention in Germany, coincident with the industrial development and the migration to the cities. Among the arguments presented for this view are that sterilizing the milk has not materially reduced infantile mortality, while the mortality fluctuates with the temperature, and especially with the temperature in the room where the child lives—this effect of heat may be evident even in winter, in overheated rooms. Rietschel (Deut. med. Woch., Oct. 5, 1911).

It is probable that bacteria play a part in summer diarrhea, but the bacterial toxicity of milk is not proved, and there is not any just analogy between the disorders due to toxic products in the milk which affect all persons alike and the condition of summer diarrhea of infants. Facts show that the disease is most prevalent when the heat conditions are most excessive and in localities where such conditions exist. It is not possible to say in what manner the heat affects the body of the child, but it seems to lower resistance and make it more susceptible to other causes. It is believed that the disorder is due to a combination of causes, excessive warmth of the house as well as the external air, in addition to infected milk and other deleterious products in the food. I. A. Abt (Jour. Amer. Med. Assoc., Oct. 28, 1911).

The almost unprecedented mortality among infants which occurred during the summer of 1911 in the larger German cities, shows that housing and environment modify greatly the general effect of summer heat on infant mortality. The mortality curves of three localities having the same climatic conditions, and in which the milk supply and general care of infants were practically identical, showed that the infant mortality of one of these localities rises higher to a marked degree during July and August than that of the other two places. In the first locality the houses were packed one against the other, the whole district congested, with no open spaces around the dwellings. The fact that the rooms and houses did not cool off during nightfall, that air currents could not vary the temperature, and that practically a heat stagnation existed accounts for the high mortality in this district. The other districts were less congested and the houses spared to some extent admitting air, and the heat was more intermittent. Long sustained, high, room temperature plus humidity and air stagnation are therefore important factors which modify the general effect of summer heat on infants. Eugen Schlesinger (Deut. med. Woch., Bd. xxxviii, S. 558, 1912).

Age.—An investigation of the age of children thus attacked reveals the fact that the great majority are under 2 years. Holt has given statistics of 3000 cases of diarrhea treated in family and dispensary practice, classified according to age. These show that, of the total number, infants under 6 months form 14 per cent.; infants from 6 to 12 months, 29 per cent.; infants from 12 to 18 months, 24 per cent.; infants from 18 to 24 months, 17 per cent., and children over 2 years, 16 per cent. In France, Lesage places the age of special liability as under 18 months, and regards the first three months, and the period between the eighth and ninth months, when weaning is generally commenced, as specially dangerous.

Study, based upon the records of deaths in the city of Montreal, of 812 cases of epidemic diarrhea among infants, showed that the majority occurred during the first five years of life, and two-thirds within the first eighteen months. The cases of epidemic diarrhea commenced about the end of May and continued through the summer, reaching their highest number in July, and finally disappearing about the middle of September. A tabulation showed that the deaths were unevenly distributed throughout the city, but bear no relation to the water supply. The areas in which most deaths occurred were those in which there was low-class property, narrow lanes, and blind alleys, together with an abundance of refuse and bad sanitary arrangements. In nearly every place there was found a small shut-in court with the houses arranged around it. The surface of the yard was usually unpaved, and there was no provision for efficient drainage. The writer believes that food is probably the chief channel by which the infection gains admission to the intestinal tract.

The area in which the disease is most frequent is low-lying as compared with the surrounding places. It is evident that such places receive subsoil drainage. Privies and cesspools are found to be a frequent source of contamination of the soil in these areas. Where the sanitary conditions in these respects have been improved epidemic diarrhea nearly disappears. T. A. Starkey (Montreal Med. Jour., July, 1904).

Overfeeding and Indigestible and Contaminated Food.—It is the experience of every physician who has kept a record of his cases that fatal, or even severe, cases of diarrhea among infants fed entirely at the breast are extremely rare. Holt emphasizes this when he says that of 1943 fatal cases of which he has collected records only 3 per cent. were breast-fed exclusively. He refers the partial immunity which, according to his statistics, infants under 6 months enjoy to the fact that the great majority of such are breast-fed, and in this way obtain a sterile and digestible food with little liability to overfeeding. With the commencement of artificial feeding, gastrointestinal disorders at once acquire prominence. Too often the food substituted for breast-milk is difficult of digestion, defective in composition, and given to the infant at too frequent intervals or in too large amounts, thus setting up indigestion and weakening the resistance of the intestinal tract to infection; nevertheless, as the experience of all testifies, the material supplied as food to the infant may be of a most faulty character, giving rise to indigestion, colic, and malnutrition, and yet during the cool season diarrhea, except of a temporary and easily controlled form, is rarely met with. The carbohydrates, especially sugar, have recently been incriminated as prominent causes during warm weather.

The alimentary intoxication of infants is a metabolic intoxication caused by the giving of food which produces toxic products of an inadequate metabolism, which may lead to fatal consequences, but disappears when the food is withheld. Certain foods, however, give rise to these effects. The writer insists on the importance of the fats and sugars in the infant's food. Proteids are comparatively harmless. The exact nature of the toxins is unknown. The condition is probably analogous to an acid intoxication, and the theory that it is due to alimentary rather than to bacterial toxins is supported by the absence of lesions in the alimentary canal, the absence of any micro-organism associated with it, the ready cure by withdrawal of food, the widely different conditions with which it is associated, and the lack of putrefactive or fermentative products that are caused by bacterial activity within the intestines. Joseph Brennemann (Jour. Amer. Med. Assoc., Feb. 27, 1909).

Excessive carbohydrate fermentation is the primary cause of severe dyspeptic disturbances, both in infants and older children. The physiologically weak intestine of the infant and the intestine of the older child, after it has been weakened by severe disease, behave alike in respect to carbohydrates. At all ages disturbances in the digestion of carbohydrates entail most readily intestinal catarrh, as the starch waste in the bowel putrefies so easily. The writer strikes milk from the diet in the diarrheas of children for at least a week after the stools are normal once more. The albuminous type of foods, with fat, but very little carbohydrates, should be the main reliance. L. F. Meyer (Therap. Monats., May, 1911).

For the chief exciting cause, therefore, of the severer diarrheas of infancy we must look farther, and such a cause, it is now generally conceded, exists in the development in the intestinal tract of toxin-producing bacteria introduced for the most part with the infant's food. The most important ingredient of an infant's food is milk, and this is particularly liable to be contaminated from many sources. Even in winter the average dairy milk is loaded with micro-organisms, but their development is checked by the low temperature. With the approach of summer, however, and the raising of the temperature at which milk is kept to 60° F., and upward, multiplication of these organisms in the milk takes place with great rapidity.

The alimentary intoxication in infants is more likely due to bacterial products in the intestine, rather than to faulty metabolism. The three recognized types are: the indolic, the saccharobutyric, and that type in which the proteids, hydrocarbons and carbohydrates are subject to bacterial decomposition. In any case the clinical syndrome known as alimentary intoxication deserves clinical recognition. Sugar is by no means a harmless substance. The old maxim that sweets may produce severe illness in children is corroborated by modern observations. The writer observed many cases of sudden collapse in children fed on condensed milk and other foods high in carbohydrate content. He feels convinced that these were cases of alimentary intoxication. Even in breast-fed infants, the collapse may occur if they are fed on other foods also. J. Zahorsky (Jour. Missouri State Med. Assoc., Dec., 1907).

In the adult the acidity of the gastric juice and the more complete digestion of the food in the stomach check the development of micro-organisms before the food enters the intestinal tract. Traube and Escherich have shown that in the infant stomach this inhibitory action is, to a great extent, wanting. During the digestive act there is no free hydrochloric acid in the infant's stomach. Both digestion and absorption take place more imperfectly in the stomach of an infant than in that of an adult and the food is quickly passed on into the small intestine, where it meets the bile and the alkaline secretions of the duodenum. There is now practically no hindrance to the development of injurious bacteria, excepting in the rapidity and completeness with which the digestive process is performed. Imperfect digestion, always slow digestion, therefore, by permitting fermentative changes furnishes the conditions under which pathogenic bacteria, introduced by means of contaminated food, or present in the canal, but previously hindered in development, may flourish and evolve their poisonous toxins.

Booker, to whom the medical world is indebted for a careful investigation of this subject, states that in infantile diarrhea the conditions for the development of bacteria in the intestinal canal appear to differ from those obtaining in the healthy intestine. The bacterial forms present a greater variety; forms met with only occasionally and in small numbers in the healthy intestine are now much more pronounced, and frequently appear in immense numbers, while the *Bacillus coli communis* and the *Bacillus lactis aërogenes* become more uniformly distributed through the intestine. No single species of micro-organism is met with sufficiently frequent to be regarded in itself as the specific cause of diarrhea; but among the many forms encountered several varieties of streptococci and the *Proteus vulgaris* appear to be of special importance. The streptococci are met with frequently; rarely seen in the stomach and upper part of the small intestine, they become much more abundant in the lower ileum and colon, especially in those cases where ulceration of the mucosa is going on. So constantly and in such large numbers are they found in these cases that it is reasonable to suppose that they play an active and important rôle in the ulcerative process. Of the *Proteus vulgaris,* Booker says that it is found in more than half of the severer cases of diarrhea; in the milder forms it is seldom seen. Cases in which this bacillus abounds present a different type of symptoms to those in which streptococci prevail; the patients more frequently show toxic phenomena and have watery or semifluid stools with a strong, offensive odor, but otherwise exhibit little evidence of serious inflammatory trouble in the intestine. More recently considerable attention has been devoted to an investigation of the *Bacillus dysenteriæ* and the part it plays in the production of dysentery. It was first studied by Shiga, and afterward by Flexner in the Philippine Islands, both of whom found it present in such a large proportion of the diarrheas of the East as to suggest a causal relation. Two distinct and important varieties have been noted, which have been named after these two investigators. More recently it has been recognized as present in a larger number of the dysenteric diarrheas in this country. A careful investigation at the Rockefeller Institute in 1903 of 412 cases of summer diarrhea showed the presence of this micro-organism in 270 cases. It was almost invariably found to be present in those cases characterized by the presence of mucus and blood in small quantities. Associated with this bacillus are numerous streptococci and bacilli of the colon group. Among other forms of bacteria possessing pathogenic properties encountered we may mention the *Staphylococcus pyogenes,* the *Bacillus pyocyaneus,* the *Bacillus mesentericus,* and the *Bacillus enteritidis* (Gärtner). Such forms probably more or less modify the symptoms in special cases.

> Two instances in different localities in which the spread of cholera was traced to two infants who had succumbed to what was supposed to be ordinary gastroenteritis but which proved to be cholera, the germs having been imported from other towns and the infants in each case being the first to contract the disease. In one case the infant died in the hospital and examination of the other children in the ward revealed cholera germs in a number of others; all the inmates of the ward and the attendants were at once isolated and further spread of infection in the institution was thus prevented. Gioseffi (Gaz. degli Ospedali, Sept. 28, 1912).

Depressed Vitality.—We may add that all conditions which lower the vitality of the infant favor gastrointestinal disturbance and impair the infant's resistance to infection. The intense heat of summer, especially when associated with great humidity, exerts a depressing action upon the nervous system of the infant, particularly upon the vasomotor system, and must, we think, be regarded as an important predisposing cause. Defective hygienic conditions, previous acute disease, and malnutrition in all its forms, especially if associated with rachitis, syphilis, and tuberculosis, act in this way. All forms of overexcitement, the nerve irritation often accompanying dentition, and reflex impulses arising from undue exposure of the lower limbs and often the abdomen of the infant to variations in temperature have all a disturbing influence in digestion, and may, therefore, be regarded as predisposing causes of diarrhea. Still more, if these conditions continue, or are frequently induced, this repetition of "insults to the intestinal mucosa" (Flexner) renders the intestine particularly liable to bacterial invasion.

> Attention is called by the writer to the cathartic property in the grasses which form the food of so many cows from spring to autumn. This property disappears when the grass is dried in the form of hay. The mortality curve follows the life of this type of vegetation, reaching its maximum in July, then gradually declining. Infants get the full physiologic effects and often the toxic effects of the aperient properties in the milk from the grass-fed cows. From October to May there is almost none of this diarrheal tendency apparent. Sterilization does not destroy this poison, which is a chemical one. The cow whose milk is used for infants should be kept off of pasture, and should be stall-fed, as in the winter. The chemistry of the grasses offers a comparatively new field for study. J. L. Walsh (Med. Rec., Sept. 15, 1906).

MORBID ANATOMY.—The anatomical lesions met with in the intestinal tract of the infant, as the result of diarrhea, are of a varied character, and are due, apparently, to the intensity of the irritant and the period of time during which its action has persisted. Nevertheless, it must be acknowledged that there is frequently a surprising want of relation between the post-mortem evidence of disease and the severity of the clinical phenomena, and *vice versâ.* Attempts have been made at a classification, but it is generally admitted that, although cases may be grouped according to the prominence attained by certain lesions, no distinct dividing lines can be drawn.

In the acute cases the lesions may be comparatively superficial. In such to the naked eye the stomach and upper portion of the small intestine appear almost normal; toward the lower end of the ileum and throughout the colon, indications of inflammatory disturbance may be seen; as a rule such are specially pronounced in the region of the sigmoid flexure. If the attack has been severe, irregular patches of local congestion are seen, with more or less swelling and hyperemia of the solitary glands and of Peyer's patches. Under the microscope hardened sections of the intestinal wall show in places loss of superficial epithelium, due, in great measure, to the irritative action of the toxins generated by the bacteria. Wherever this erosion has taken place an invasion of the mucosa may follow. This condition is especially noticeable toward the lower portion of the ileum and over the whole of the colon, where a considerable infiltration of the mucosa may frequently be seen. In a few instances signs of an acute general infection are presented by fatty degeneration and necrosis of cells in the liver, by the presence of lobular pneumonia, and by necrosis of the epithelium in the convoluted and irregular tubules of the kidney.

> The result of experiments by the writer shows that the glycolytic power of the tissues of the nursling is relatively high, since the quantity of sugar so convertible varied between 50 and 80 cm. per kilogram of weight, while the liver arrests only about 4 or 5 Gm.; that inversely with

what is observed in the liver the glycolytic power of the tissues remains about constant, whether the experiment be made upon a healthy infant or upon one suffering from gastroenteritis; that, consequently, it is not necessary to take into account this possible source of error in investigating alimentary glycosuria in the nursling. Terrien (Revue mensuelle des mal. de l'enfance., Jan., 1901).

The urinary findings in a series of infants under constant observation in hospital wards showed that in 22 the urine was abnormal; it contained albumin and occasionally hyaline casts as the only pathological element in 7 instances (febrile or toxic albuminuria); in 7 others the presence of pus cells was the chief characteristic (pyuria-pyelitis); in the remaining 8 cases albumin, casts, and pus were all present, indicative of nephritis or pyelonephritis. The urinary changes were more frequent in ileocolitis, than in dyspeptic or fermental diarrhea, though the extent of renal involvement seemed to depend less on the variety of the intestinal infection and more on its intensity. The pyuria persisted in some instances without apparently interfering with convalescence; in others it yielded to urotropin, and in still others it devloped into a serious and fatal complication. The infection seemed to have its origin in the intestinal canal, whence it reached the kidney either through the blood- or lymph- streams, or by contiguity of structure. There was no evidence of involvement of the urethra or bladder or of ascending infection. The few autopsies made indicated clearly that although the kidneys frequently escape injury during enteritis, they become the seat of extensive secondary changes in this as in other forms of infection. The renal changes during intestinal diseases in infections seemed to be those of degeneration (parenchymatous, hyaline, and fatty) of the convoluted tubules rather than those of focal infection. In 19 cases suffering from ailments other than intestinal infection, and for the most part less acute in character, no urinary abnormalities were discernible. J. H. M. Knox and J. C. Meakins (Arch. Int. Med., vol ii, p. 241, 1908).

Hohlfeld, in a number of investigations, found that in the majority of fatal gastroenteric cases the urine contained albumin and a few casts. In 35 autopsies the changes in the kidneys were found to be parenchymatous. He believes that toxemia and kidney irritation react on each other and offer a bad prognosis. Chapin, in 86 cases, records 75 as having albumin and casts in the urine; also the majority of the fatal cases had albumin in the urine. The authors tested the urine in 300 babies suffering from gastrointestinal conditions. The examinations were consecutive. The tests for albumin were nitric acid (cold), acetic acid and heat, or both. In children with chronic digestive disturbances albumin was found in but 8 per cent. There was usually only a trace of it, with no casts and no edema. The presence of the albumin had no effect on the prognosis. In acute conditions albumin was found in a little over 10 per cent. of the cases. There was usually only a trace of it without casts or blood and this had no effect on prognosis. The mortality was considerably higher in the intestinal cases with albumin than without it. These were not accompanied by edema. The authors conclude that the pathological condition in the kidneys does not progress beyond cloudy swelling or acute hyperemia. There was nothing to suggest any causative relation between the affection of the kidneys and stupor, restlessness and convulsions. These they believe are due to toxemia and not to uremia. J. L. Morse and Bronson Crothers (Archives of Pediatrics, Aug., 1909).

In another class of cases the inflammatory changes are more pronounced. In a proportion of these the lesions may be described as catarrhal in character.

The macroscopic changes are, to a great extent, confined to the lower end of the ileum and to the colon, where the congestion may be very marked; in some cases quite general; in others localized in patches. The lymph-nodules are enlarged and can frequently be seen with commencing ulceration at their summit; Peyer's patches are swollen and hyperemic. Under the microsope hardened sections from the stomach and the small intestine reveal marked cloudiness of the epithelial cells, and in places loss of superficial epithelium. The connective tissue of the villi and that supporting the glands of Lieberkühn are more or less densely infiltrated. The ducts contain an excess of goblet-cells and are distended with mucus. The loss of superficial epithelium is extensive throughout the colon. Associated with it is a more or less dense infiltration of the mucosa, an infiltration which, in places, may extend even to the muscular coat. Should the duration of the attack be further protracted, ulceration may supervene, chiefly in the colon, rarely in the lower portion of the ileum. Such ulceration is, for the most part, superficial, rarely extending deeper than the mucosa. The ulcers, in general, are circular, but in the more severe cases several ulcers may coalesce, forming large, irregular patches, two to three inches in diameter.

In the cadavers of 10 infants the inflammation in the intestinal mucosa had been mainly restricted to the ileocecal valve. It rarely extended into the small intestine and then but a short distance. In the large intestine the inflammation spread more. In a few cases there was slight inflammation in the duodenum, but, as a rule, the small intestine was free from any decided inflammation. The superficial epithelium and the glands were generally in good order. C. E. Bloch (Jahrbuch f. Kinderheilkunde, Bd. lviii, No. 5, 1905).

In another group of this class the intensity of the inflammation appears to fall chiefly upon the lymph-nodules, which throughout the colon, and especially in the neighborhood of the sigmoid flexure, show indications of a destructive inflammation. Under the microscope they are seen to be swollen and infiltrated, many showing focal necroses. The surrounding tissues are deeply infiltrated with lymphoid cells. In time they break down, forming small, but deep ulcers, with overhanging edges, exhibiting a tendency to extend chiefly in the submucous tissue. In a few cases, fortunately rare, the inflammation of the colon is of such an intense fibrinous character as to lead to necrosis with the formation of pseudomembrane.

In a report of 54 cases of children, ranging from 2½ months to 4 years, with digestive diseases, the gastric juice was examined 119 times, both qualitatively and quantitatively. Of the children 6 had dyspepsia; 11 acute gastroenteritis; 6 acute enteritis; 5 acute colitis, and 26 chronic gastrointestinal disorders. Absorption occurs more rapidly under than over 4 years of age. Absorption is most affected in acute gastroenteritis, next in dyspepsia. The stomach is least affected in acute dyspepsia and enteritis; most affected in acute gastroenteritis and chronic diseases. T. von Hecker (Jahrbuch f. Kinderheilk., Nov., 1902).

The leucocytes in a large number of cases of infant diarrhea showed that there is an increase in the number of leucocytes in nearly every case, but the increase is too variable to be of any diagnostic importance. There is, however, one change which stands out prominently, and that is the relative increase in the polymorphonuclears and the decrease in the lymphocytes. This is of importance, because it is found to be of value in prognosticating the severity of the attack. A marked increase in the number of polynuclear leucocytes means that the child is badly poisoned, whatever the other signs may indicate. J. Zahorsky (N. Y. Med. Jour., Sept. 12, 1903).

CLASSIFICATION.—Attempts have been made at a classification of diarrheal disorders, based either upon the changes found *post mortem* in the intestinal canal or upon the bacteriological conditions met with in the discharges, but in both respects our knowledge is still too imperfect to permit us from it to draw dividing lines in a satisfactory manner. Attempts have also been made to recognize certain clinical types of the disease, but it must be admitted that our clinical types have no sharp dividing lines, and, both in the group and in the individual, they show a tendency to pass from the milder into the more severe form.

Two classifications, which rest partly on a pathological and partly upon a clinical basis, are worthy of mention. One is that of Lesage, who groups the acute cases of infantile diarrhea into three classes. In the first he includes all those which are due to the presence in the infant's food, whether breast- or cows' milk, of irritant substances not the result of fermentation in the milk. These diarrheas are generally of a mild type and quickly controlled. In a second group are placed those cases where the disturbance is due to fermentation in the stomach or intestinal canal of indigestible, but at the same time more or less sterile, food. The constitutional intoxication in these cases is due to the abnormal development and some times increase in virulence of bacteria previously existing in the canal (endogenous). These cases, although sometimes severe, generally run a comparatively mild course. The third and largest group contains all those cases in which the diarrhea is due to bacteria and their toxins present in the milk administered as food to the infant (exogenous). The constitutional symptoms met with in this class are frequently of the severest type.

Booker also groups the acute cases of diarrhea met with during summer into three classes. In the first he places all cases of a dyspeptic and non-inflammatory character. In these the stools are lumpy, acid, and contain no leucocytes or epithelial cells; the bacteria are only those of normal healthy motions, and the diarrhea is of a mild form and, for the most part, easily controlled; however, if neglected, it shows a tendency to take on the characters of one of the two succeeding classes. The second group is characterized chiefly by symptoms of a systemic intoxication, with which is associated a variable amount of local inflammation; the stools are frequent, much altered in color and consistence, and contain curds and an increase of mucus. Seldom any one form of bacteria is so greatly in excess as to exclude the influence of other forms. In a third group of cases local inflammatory symptoms are prominent; the stools are frequent, contain much mucus, and sometimes blood; streptococci are found in predominating numbers, although other forms of bacteria are also present. In the more severe cases an invasion of the tissues of the intestinal wall by bacteria takes place, and in many instances more or less extensive ulceration of a suppurative character may be found *post mortem*. There is, according to Booker, a considerable difference in the clinical course run by the individual cases in this group; some patients respond readily to treatment, while others are little influenced and steadily grow worse, until the disease terminates fatally. Booker thinks that this may possibly be due to the fact that the streptococci met with are of more than one variety.

While typical instances of these three groups may be easily recognized, there are many transitional cases which do not fall into any one of them, and are probably due to a more mixed infection in which no one micro-organism is especially predominant.

This classification of Booker's corresponds clinically very closely with that of Holt, who, however, lays more emphasis on the anatomical post-mortem changes.

To these groups we must add a fourth, comprising those cases which assume a chronic type, and are not infrequently met with as the sequelæ of one of the preceding forms. With this group, as with the others, we can draw no definite dividing line separating it sharply from the more acute cases. Holt terms those cases chronic which have persisted longer than six weeks. Some cases, however, beginning acutely, assume the type of chronicity sooner even than this. In these the activity of the inflammation subsides, the appetite partially returns, but the diarrhea though lessened persists; in some maintained by a varying amount of ulceration of the intestinal wall; in others by a more or less atrophic condition of the intestinal glands. In the latter case the progressive emaciation indicates how serious is the interference with the processes of digestion and absorption.

These somewhat provisional groups may be tabulated as follows:—

1. Functional diarrheas non-inflammatory in character.

2. Inflammatory diarrheas in which the symptoms of a toxic systemic infection are predominant.

3. Inflammatory diarrheas in which, in addition to the systemic infection, the symptoms of an acute local inflammation have a prominent part.

4. Chronic diarrheas in which the acute inflammatory symptoms have more or less subsided, but in which the stools remain abnormal, both in character and frequency, and emaciation is apt to supervene.

FUNCTIONAL DIARRHEAS.—Many cases of infantile diarrhea are met with which must be regarded as functional rather than inflammatory in character. During dentition a moderate increase in peristalsis and secretion is sometimes noted which it is difficult to attribute to any fault in diet, and which promptly subsides on the eruption of the teeth. In a few instances a similar condition may be induced by impulses acting through the nervous system, such as fright, overexcitement, and a sudden chill to the surface of the body. At other times these same causes act chiefly by disturbing digestion. Substances also may occasionally be given as food to the infant which act as direct mechanical irritants to the sensitive mucous membrane of the alimentary tract.

In this group are also to be placed many diarrheas met with in breast-fed infants, where, owing to a faulty dietary or mode of life, or to a nervous overstrain on the part of the mother or nurse, the breast-milk becomes altered, resulting in either gastric or intestinal indigestion in the infant, followed by diarrhea. The time of weaning is apt to be associated with a similar irritability. This liability is still further increased by all conditions which lower the tone of the nervous centers.

Symptoms.—In some instances the diarrhea may commence quite suddenly with large, more or less fluid motions, containing, besides fecal matter, considerable undigested material. In other cases symptoms of gastric irritation and abdominal pain precede, for some hours, the diarrhea. Examination of the infant generally reveals a moderate amount of pyrexia: 100° to 103° F. (37.8° to 39.4° C.); rarely does the temperature run higher, except in cases of sudden onset with severe gastric disturbance. Slight abdominal distention may often be noted. The stools are frequent, thin, usually sour-smelling, and of varying color. In young infants on an exclusive milk diet they are, in general, of some shade of green and of a distinctly acid reaction; occasionally, however, they are gray or chalky in color and frothy in character. In older infants on a more mixed diet the stools may have no uniform color, but be in part green and in part some shade of brown. Undigested food is always present in the form of casein masses, or smaller and softer masses, consisting of fat curds or soaps. Examination of the stools under the microscope reveals only those forms of bacteria met with in normal feces. The infant is peevish and may either refuse its food altogether or drink greedily only to allay its feverish thirst. Should the pyrexia run high nervous symptoms may manifest themselves, *e.g.*, twitching of the limbs, great restlessness, and wakefulness.

Food fever in children consists of an attack of fever which comes on suddenly, is accompanied by signs, more or less pronounced, of digestive disturbance, lasts in its acute form for several days, and may linger on in a modified degree for some weeks. If the attacks occur frequently, once a month or so, their effect upon the nutrition of the patient is highly injurious. The subjects of the complaint are usually neurotic children of either sex between the ages of 3 or 4 and 10 or 12 years. The attack begins with headache, sometimes with vomiting, sometimes with diarrhea. The temperature rises to from 101° F. to 105° F. (38.3° C. to 40.5° C.); it is usually reduced by a dose of calomel, but rises again. The cases are probably primarily attacks of acute gastric catarrh. The persistence of the fever is due to reabsorption from the bowel of injurious products of decomposition. To prevent and cut short the attacks a careful diet is of the utmost importance. Excess of carbohydrates and articles of food capable of undergoing unwholesome fermentation in the bowel, should be forbidden. Milk, except in limited quantity, is harmful. The proper diet for these children consists of mutton, poultry, white fish, well-boiled green vegetables, and eggs, plenty of butter and stale bread, and the salted foods —such as bacon. Smith (Brit. Med. Jour., Feb. 10, 1906).

"Soapy stools" indicate always some chronic disturbance in the absorption of fat. At the same time the splitting of the fat proceeds unhindered, and there cannot be much acidity or increased peristalsis or catarrhal irritation. In case of acute exacerbations, "soapy stools" give way to other forms of fat stools, but after the acute phase has subsided the soapy stools return. Hecht (Münch. med. Woch., May 12, 1908).

Large curds in infants' stools are composed of some proteid (probably casein or one of its derivatives), which on coagulating entangles the milk fat in its meshes. The amount of fat in the curds depends on the amount of fat in the milk, and as this fat increases it replaces the proteid in the curd. The presence of large curds, which has been taken by some investigators to indicate an increase of gastric HCl, can with as great probability be interpreted as indicating a lack of HCl. Talbot (Boston Med. and Surg. Jour., June 11, 1908).

The attack in this type of the disease is generally of brief duration. After the diarrhea has continued for twelve or twenty-four hours the temperature generally falls; nervous symptoms, if present, pass away; the motions in a few days become less frequent and gradually resume their normal appearance, and the desire for food becomes more imperative.

Diagnosis.—At the onset, unless from the history of the case, it is impossible to predict with certainty just what we may have to deal with. It must be remembered that symptoms similar to the above may not infrequently usher in a severe constitutional disorder.

Prognosis.—Simple functional diarrhea, unless in infants of the weakest constitution, can never be regarded as presenting much cause for anxiety. The danger lies in neglect. An injudicious dietary, especially in hot weather, may prolong the attack or convert it into one of the inflammatory forms of the disease.

Treatment.—In cases in which the diarrhea appears to have removed the irritant, it will suffice to secure absolute rest to the alimentary tract for a period varying from twelve to twenty-four hours, permitting only sterile water in small quantities as frequently as may be desired. In the majority of instances, however, it is wiser to secure at the outset, by means of medicine, a thorough evacuation of the bowels, ridding them in this way of any fermenting material. To accomplish this we may make use of either **castor oil** or **calomel**, both of which act promptly and with little irritant effect on the mucous membrane. Of the former a full dose may be given in any convenient way.

Should there be much gastric irritation, as shown by a tendency to retch or vomit, the latter is preferable, and may be given in small doses (1/8 to 1/4 grain—0.008 to 0.016 Gm.) at intervals of half an hour or of an hour until a decided effect is obtained. Afterward, if necessary, one of the preparations of bismuth, preferably **bismuth carbonate**, with a small quantity of some opiate, may be given for a few days. If the attack has been of a mild character, a thin **rice** or **barley water** containing a small amount of **sugar of milk** may be allowed after the first twelve hours have passed. Stimulants in the form of **whisky** or **brandy** are to be given only if indications of prostration make their appearance. In the majority of cases this dietary may be increased after thirty-six or forty-eight hours. In infants who are breast-fed, a limited nursing may be allowed, permitting the infant to take a little more than half its usual quantity at each nursing. **Rice water** or weak **albumin water** may be given between times. In those artificially fed the food for several days must be weak in character and limited in amount. A small quantity of a fat-free milk may be added to the rice or barley water after the third day.

The writer advocates the following measures: 1. Diet. *a.* Artificially fed. Stop all milk and give either barley- or granum- water, made by mixing 1 heaping teaspoonful of the flour with 1 pint of water, cooking for fifteen minutes, and adding salt; feed every two or three hours, according to age. Also give 2 ounces of boiled water between meals. Continue this plan of feeding for twenty-four or forty-eight hours, then add 1 ounce of whole milk to each pint of gruel, and gradually increase milk till correct amount for child's age and digestive capacity reached. Where fat in fresh milk not tolerated after the diarrhea, substitute condensed milk, 1 part to 30 of the gruel, gradually increased to 1 to 10 or 12; later resume fresh milk little by little. In babies 1 to 2 years old mutton or chicken broths, free from fat, may be given in addition once or twice daily; also a little zwieback broken up in the broth; after two or three days, farina porridge. Avoid strong, thick gruels. *b.* Breast-fed. Barley water for twenty-four hours; also boiled water. Mother to use breast-pump at regular intervals. Later, 1 or 2 ounces barley water given just before breast-feeding, and nursing allowed five minutes only. As stools improve, barley water decreased and breast-nursing increased. 2. Drug medication. For diarrhea: **Castor oil,** ʒj-ij (4 to 8 c.c.), followed next day by **aromatic spirit of rhubarb,** 5 to 20 drops (0.3 to 1.25 c.c.) every three hours. Continue this two or three days. If stools still frequent, with blood or much mucus, give **calomel,** 1/10 grain (0.0065 Gm.) every hour for 10 doses, and follow, after several free movements, by **bismuth mixture:**

℞ *Olei ricini* .... fʒiiss (10 c.c.).
Bismuthi subnitratis. ʒv (20 Gm.).
Mucilaginis acaciæ.. f℥ij (60 c.c.).
Aquæ cinnamomi,
q. s. ad........... f℥vj (180 c.c.).

M. Sig.: One teaspoonful every three hours.

℞ *Bismuthi salicylatis* .... gr. xij (0.8 Gm.).
Bismuthi subnitratis .... ʒv (20 Gm.).
Syrupi rhei aromatici .... fʒij (8 c.c.).
Aquæ.....q. s. ad f℥iv (120 c.c.).

M. Sig.: One teaspoonful every three hours.

Where stimulation needed: **Liquid peptonoids,** 20 drops to 1 dram (1.25 to 4 c.c.) in water or gruel; rarely, **albumin water** with 1 dram (4 c.c.) of **brandy** to ½ pint (240 c.c.). Where fever, much mucus or blood in stools: Irrigation of bowel with **normal saline solution** at 98° F. (36.7° C.). If blood several days in succession: High irrigation, through rectal catheter, with **tannic acid,** 1 teaspoonful to a quart of boiled water. 3. Hygiene: Keep baby in **open air** as much as possible. Frequent **cool sponge baths** to which a little **alcohol** added where fever. Collidge (Bull. Lying-in Hosp., New York City, vol. vii, No. 1, 1911).

Diet for infants in cases characterized as follows: After twenty-four to forty-eight hours of fever, there comes a stage when the infant has 8 to 10 mucous, curdy, green and sometimes bloody stools a day; the weight continually decreases, though not showing the marked loss which accompanied the onset, and the temperature ranges between 99° F. (37.2° C.) and 101° F. (38.3° C.). In this condition, called by many a "putrefactive diarrhea," the diet to be chosen must be one which will not affect adversely the workings of a very much deranged internal metabolism, and which at the same time will form the least suitable medium for a bacterial infection of the colon. It is altogether likely, and is in agreement with the views of most writers, that the substance for such bacteria to grow in, which must of course be proteid in character, is the mucus secreted by the intestinal wall, and not the proteid of the food. Any irritating food must therefore be avoided, as, by causing an increased flow of mucus, it will favor bacterial pullulation.

The proteid of cows' milk is that food, in all instances, which is the least irritating to the intestine, and therefore advisable in these cases. It is best obtained by removing the whey from skimmed milk by means of coagulation with chymogen or pepsin. The curd is then broken up into fine particles by passing through a colander several times. To suspend the curd for administration to the infant, the author has found 5 per cent. **gelatin** water very useful. There are two objections to it, viz., there is a tendency to the subsequent formation of lumps, and the preparation solidifies on cooling, having therefore to be heated before use, with the possibility of coagulating the curd into a hard mass. But in spite of these objections, the writer has found the solution to give very good results, after the initial barley-water period of twenty-four to forty-eight hours.

At the most, four or five days to a week is as long as the above wholly proteid food can be used. After this it is well to add a certain amount of **buttermilk** in place of the gelatin water, and gradually replace the skimmed-milk curds with whole-milk curds, gradually getting the child upon an **albumin milk,** and then turning to a whole-milk mixture. By this method of treatment, one can reduce very markedly the sugar content of the food. C. G. Grulee (Interstate Med. Jour., Jan., 1913).

General measures, such as physical rest, with freedom from all forms of excitement, **frequent bathing** with water graduated in temperature to suit the condition of the infant, and abundance of **fresh air** are all important in the management of these cases.

INFLAMMATORY DIARRHEAS: SUMMER COMPLAINT OF INFANTS.

The two groups of inflammatory diarrheas include the great majority of cases of infantile diarrhea met with during the summer months. They are very closely allied in their etiology, and, although the intestinal lesions in the one are comparatively slight, while the symptoms of local inflammation in the other become prominent, in both we have to deal with marked constitutional disturbance. All that has been said in reference to the influence of age, of season, and of the mode of feeding is equally true of both groups. The symptoms and course of these two varieties of the disease differ in important particulars.

INFLAMMATORY DIARRHEAS in which the Symptoms of a Toxic Systemic Infection are Predominant; ACUTE GASTROENTERIC INFECTION: ACUTE GASTROINTESTINAL CATARRH.

Symptoms.—As might be expected, when we consider the various ways and the varying numbers and characters with which these toxin-producing bacteria make their entrance into the alimentary tract and the different conditions under which their development may take place in the stomach and intestine, the mode of onset of this disease is very variable. Frequently it is gradual; the symptoms present little except their persistence to distinguish them from those produced by indigestion. The infant may be fretful, show occasional signs of colic, be restless at night, and slightly feverish, and associated with these disturbances may be some looseness of the bowels. As the disease progresses the symptoms increase in severity; the motions become frequent, thin in character, of a sour, or, more generally, of an offensive odor; their color is variable, generally some shade of green, due to an alteration in the bile-pigment, the exact nature of which is still uncertain; pyrexia increases, the pulse becomes quick and weak, and pain becomes a marked feature, interfering with rest and sleep.

Green stools are distinguished not only by their color, but by the presence of considerable mucus. This is due to the action of a substance which the writer has isolated from such stools, and regards as a ferment. It oxidizes guaiacol in presence of hydrogen dioxide, but the reaction does not occur if the stool is first heated to boiling point. The oxidation causes a brownish discoloration which is most marked in the flakes of mucus and is not diffuse. The substance is contained in the mucus and apparently has an oxidizing action on bilirubin. Wernstedt (Hygiea, vol. lxvii, No. 8, 1905).

The degree of oxidation of the biliary coloring matter in the stools of infants does not depend wholly on the oxydase, but a distinct influence is exerted on the coloring by the very uncertain, but usually significant reducing power of the bacteria in the stool. The oxydase can certainly develop its action only when the reduction process is so insignificant that the biliary coloring matter is unaffected. If the reducing power is increased in intensity the stool always contains somewhat reduced biliary coloring matter, pre-eminently bilirubin. The intestinal bacteria then hinder the oxidation of the biliary coloring matter so that such stools contain bilirubin in spite of the amount of oxydases. Hecht (Münch. med. Woch., June 11, 1907).

In other cases grave symptoms appear suddenly in an infant who has previously been well or only slightly ailing. The temperature rises rapidly to 104° or 105° F. (40° to 40.5° C.), with either unusual drowsiness or great restlessness, and signs of distress. Vomiting may set in early and continue in a most persistent manner. In some instances alarming nervous symptoms may develop, such as stupor, great excitement, or even convulsions. After several loose movements have occurred the temperature may fall 1 or 2 degrees, and the nervous symptoms pass off to a great extent. Frequent loose movements, with much colicky pain and considerable prostration, now make their appearance.

When the disease is well established the symptoms become very characteristic: the infant is restless, moaning or crying frequently; the face is pale and its features somewhat pinched; the eyes sunken; the tongue coated in the center, but with tip and edges red and dry; thirst is pronounced, but fluids are frequently vomited shortly after they are taken; the abdomen is generally, but not always, distended. Occasionally we may distinguish through the thin abdominal wall marked distention of the stomach or of the small or large bowel. The skin gradually assumes a harsh feeling, while the subcutaneous tissues waste rapidly; the temperature varies from 102° F. (38.9° C.) in the morning to 103° F. (39.4° C.) or more in the evening, and the quick and feeble pulse indicates great exhaustion. Pain, to a greater or less extent, is always present, but exacerbations may be noted shortly before each evacuation. Abdominal tenderness is not marked, but exists in some cases. The stools continue to be frequent, often almost entirely fluid, and of a varying color, green or brown; they have a sour, more generally an offensive odor, and contain an excess of mucus. Little useful diagnostic information can be gained from their appearance, but we may consider that frequent and very fluid stools indicate a severe attack. The reaction is, in the beginning, always acid, but in the more severe cases becomes neutral or even alkaline. Lesage says that a relation generally exists between the character of the reaction and the degree of the infection. Under the microscope the stools are seen to contain undigested food, epithelial cells, few, if any, leucocytes, and numerous bacteria, among which bacilli predominate. As the disease progresses the vomiting becomes less urgent, the pain appears to be less acutely felt, the pulse becomes weaker, emaciation proceeds rapidly, and the urine becomes scanty and not infrequently shows the presence of a small amount of albumin.

Should the disease proceed to an unfavorable termination the general prostration increases; the extremities become cold, slightly cyanosed, and sometimes edematous; the slightly swollen eyelids only half close over the deep-sunken eyes; the fontanelle, if still open, is much depressed; the infant ceases to cry, and death closes the scene generally in a very quiet manner.

Under wise and energetic treatment, however, begun early, the course of the attack may be aborted or much shortened, particularly in infants with a previously good digestive record. In some, although the severity of the symptoms may abate, the diarrhea persists and indications of a modified ileocolitis make their appearance.

Relapses are not uncommon, due, most frequently, to some error in dietary, usually that of allowing milk too early and in too strong a modification. Occasionally they appear to arise from the nervous and cardiac depression produced by a wave of intense heat.

Complications.—In the more severe cases complications are frequently met with. Unless care is exercised, thrush is apt to appear in the mouth and spread rapidly. While in itself of slight import, it may, owing to an accompanying stomatitis, still further increase the difficulties of feeding.

Symptoms in the respiratory system in many cases develop early. Fenwick states that in 87 per cent. of his cases signs of bronchitis were present at the end of the fourth day; pneumonic consolidation was encountered in 37 per cent. To us in America these figures appear high. The onset of the bronchopneumonia is, however, often very insidious; the cough may be only slight, but the respirations will be observed to be unduly frequent, and the temperature shows a distinct rise. The physical signs are generally obscure, and most frequently are localized at the base of the lungs. The progress of the pulmonary lesion is modified by the general symptoms of the case; increased dyspnea is often a symptom of grave import. Pleurisy is very seldom observed; when it does manifest itself it tends rapidly to become purulent.

Associated sometimes with the pulmonary infection, but occasionally as a complication by itself, we meet with cerebral symptoms, stupor, delirium, or convulsions. Only rarely do we observe definite signs of local irritation, such as strabismus, inequality of pupils, and irregular pulse and respiration. Lesage makes reference to a form of paralysis which disappears with returning health. Thrombosis of the cerebral vessels may take place in the final stages, and may or may not manifest its presence by special symptoms. Still states that it was noted in 1 per cent. of the autopsies on cases of infantile diarrhea at the Children's Hospital, Great Ormond Street, London. Occasionally an attack of tetany may supervene. Should the drain of fluid from the tissues have been great, the defective circulation in the brain may of itself give rise to many of the above symptoms. Only occasionally must the cerebral symptoms be regarded as of a uremic nature.

Otitis media is to be remembered as a not infrequent complication which may give rise to retraction of the head and symptoms closely resembling meningitis (Still). Any exhausting disease, it would appear, brings with it a special liability to catarrh of the middle ear, sometimes with external discharge, sometimes without, but in either case adding fresh symptoms to those of the primary disease. Still states that in 79 consecutive autopsies on infants under 2 years pus in one or both ears was found in 32. He thinks it probable that the symptoms described as spurious hydrocephalus may, in some instances, be due to middle-ear inflammation rather than to a toxemia.

Convulsions are always to be regarded as a grave complication, but are not necessarily fatal. Their import is more serious in the later stages of the disease than at the onset.

A true parenchymatous nephritis due to infection would appear to be a rare complication. Kjellberg states he met with it in 47 per cent. of his fatal cases; but competent observers, both English and American, have failed to meet with it, except very occasionally. Fenwick states that albumin in the urine was noted in 17 per cent. of his cases before the fifth day of the disease; but in no instance did the urine show more than a trace. Under the microscope he never observed either blood-corpuscles or epithelial casts. Booker states that necrosis of the epithelium in the convoluted and straight tubules was found in nearly all his cases, and, in not a few, hyaline tube-casts were demonstrable. Infiltration with leucocytes was not seen in any case.

Edema, especially of the extremities, not infrequently makes its appearance about the second or third week of the attack. It is most common in the subacute cases, in which the symptoms show a tendency to recur. The edema is generally localized to the back of the hands, feet, and thighs. It sometimes spreads to the face. In a few instances it is associated with tenderness and then presents a close resemblance to infantile scurvy. Heubner attributes the appearance of edema to a retention of the chlorides and states that it disappears when the infant is fed on a dietary in which the chlorides are greatly reduced. The exact etiology of it, however, is still uncertain.

In a small number of cases purpura may make its appearance in infants in whom much wasting has occurred; it is always to be regarded as a very grave complication, but it is not necessarily fatal.

> Purpura is a symptom of infective diarrhea in children which is usually overlooked. Of 100 cases of diarrhea, 11 showed purpura, all of which resulted fatally. All but 2 patients were under 11 months of age. In 8 the eruption was on the abdomen, especially the lower part, and in 4 of these the thorax was also affected. The extremities, where ordinary purpura is more commonly seen, were almost always spared. The purpura was usually a late phenomenon, appearing, on an average, on the thirty-fourth day, one week before the average time of death. It is therefore connected, the author points out, with cachexia rather than acute infection of toxemia. In one patient, however, the rash disappeared and the child improved, but the diarrhea later returned and proved fatal two weeks after the disappearance of the eruption. Transfusion or the administration of horse or other serum could not have been the cause of the purpura, as the latter usually preceded these measures. Nor did the cases suggest any close relation between purpura and the edema which sometimes occurs in children after gastroenteritis. H. D. Rolleston and J. B. Molony (Proceed. of the Royal Soc. of Med., Dec., 1911).

Diagnosis.—While there may be, for the first two or three days, some uncertainty in reference to the character of a diarrhea, a persistent high temperature beyond this period stamps the attack as of an inflammatory nature. After this date fluid evacuations of an offensive odor are characteristic of the toxic form, while small stools passed with much straining and containing mucus and some blood are met with in those cases in which the local inflammatory condition is prominent. Typhoid fever is seldom met with during infancy; its onset is occasionally somewhat abrupt, but after the first few days its course becomes more characteristic. Widal's test should be applied in doubtful cases. Several of the acute specific fevers are sometimes ushered in by an intestinal disturbance, which may, for two or three days, be misleading; of these, scarlet fever and pneumonia are probably the most important.

Prognosis.—In infants suffering from chronic dyspeptic troubles, or in those whose nutrition is seriously impaired, the prognosis must always be grave. During the heat of summer an attack of inflammatory diarrhea is of much more serious import than one occurring during the cooler months of the year. In the course of an attack a decrease in the temperature and in the frequency of the stools are favorable symptoms, especially when associated with an improvement of the general appearance, an increase in the amount of urine, and perhaps an increased desire for food. On the other hand, a higher temperature, more frequent and more watery movements, a more anxious expression on the features, sighing and irregular respirations, a feeble and intermittent pulse, suppression of the urine, and the onset of nervous symptoms must all be regarded as of grave significance. In every attack of inflammatory diarrhea the prognosis is greatly dependent upon the establishment of correct treatment before the production of serious intestinal lesions.

Treatment.—Regarding this disorder as due to an intoxication of the system, either induced suddenly by an absorption from the intestinal tract of toxins in large amount or coming on gradually, owing to the development in the intestinal canal of pathogenic bacteria with a subsequent absorption of toxins, our first efforts should be directed to securing, as promptly and as effectually as possible, the clearing out of the intestinal tract. This we endeavor to effect by means of promptly acting **purgatives**, and by **lavage of the stomach and large intestines**; the small intestines we only reach by means of purgatives.

At the same time the development of bacteria should be checked by withholding food in which they can grow. Milk food, in which we know they develop very rapidly, should be forbidden for many days. Sterile water only should be allowed for the first twenty-four hours. During the early days no astringent drug is to be given to check peristalsis, at this period to be regarded as salutary in character. For the evacuation of the intestinal tract two drugs especially commend themselves on account of their prompt action and of the very slight amount of irritation which they induce. These are **castor oil** and **calomel**. Castor oil is of much value if it can be taken and retained. A full dose, 1 or 2 drams (4 to 8 Gm.), may be given in any convenient way. In many cases, however, there is too great irritability of the stomach for us to attempt the administration of this somewhat nauseous drug, and we can, with advantage, have recourse to calomel, which acts not only as a purgative, but also, to some extent, as an intestinal antiseptic. It may be given either in one full purgative dose or in a series of small doses, repeated at short intervals. Lesage recommends that if the onset is with high fever, a foul-smelling but not abundant diarrhea, and a considerable amount of tympanites a dose of 1 grain (0.065 Gm.) for an infant under 1 year, and 2 grains (0.13 Gm.) for an infant over that age, should be administered, mixed with a little sugar, in a powder. In those cases where the fever is only moderate, where the abdomen is soft and not distended, and the diarrhea is copious, small doses of 1/10 to 1/5 of a grain (0.006 to 0.013 Gm.) may be given every half-hour or hour for ten or twelve doses. Other purgatives have been employed, but, in our opinion, they are not so satisfactory.

> In a series of 200 cases, the writer found that, in 35 to 40 per cent., **bichloride of mercury**, administered to the nursing mother in doses of 1/32 grain (0.002 Gm.) three times a day, had a decided influence upon the gastrointestinal condition and nutrition of the infant. Vomiting, when not due to overfeeding or organic disease, ceased as a rule within twenty-four hours after the treatment was begun; diarrhea was always markedly improved, the frequent, foul-smelling stools containing undigested curds being rapidly replaced by the normal ones. Constipation was in like manner improved by diminishing or increasing the amount of mercury given to the mother. Colic was benefited and the weight was improved in many cases.
>
> This treatment is indicated in any gastrointestinal disturbance of the nursling. It is a harmless procedure even where no benefit results. The effect of the drug upon the non-syphilitic mother is practically *nil*, while in the syphilitic mother it improves the general condition. S. V. Haas (Archives of Pediatrics, July, 1912).

Should vomiting be severe and persistent a careful **lavage of the stomach** will often at this period of the disease prove of much value not only because it removes fermenting material and toxins, but because it has a direct sedative action on the gastric mucous membrane. This lavage can easily be accomplished by means of a few feet of rubber tubing to which is attached at one end a soft-rubber catheter (No. 15 or No. 18 English, or No. 30 Charrière), and to the other a small glass funnel. The fluid used may be either sterile water or **normal saline solution**, at a temperature of about 100° F. (37.8° C.). Three or four ounces should be introduced at a time and allowed to escape. This should be repeated until the water returns clear. Occasionally one of the milder antiseptics is added to the solution; we are convinced, however, that the use of them in this way is associated with a definite risk of absorption of an overdose, which more than counterbalances any possible advantage.

Either at the same time or a few hours later when the purgative begins to act, an effort should be made to wash out the colon. The infant should be placed on its back with its hips well elevated, and a **normal saline solution** at a temperature of 98° F. (36.7° C.) be allowed to flow slowly into the intestines through a large-sized rubber catheter introduced for six or eight inches. The pressure in the tube should be slight, the reservoir not being higher than one or two feet above the hips of the patient. If the hips are sufficiently elevated, a little gentle massage over the region of the sigmoid flexure secures the free passage of the fluid into the descending colon, and then its entrance into the transverse and ascending colon. Should the pyrexia of the infant be high, after the current has been once established the temperature of the water may be lowered to 80° F. (26.7° C.). Lower than this has been recommended by some physicians, but the very interesting experiments of R. Coleman Kemp warn us that we may in this way produce too much depression. The injection should be continued until the water returns clear. If done carefully, the pulse, after the injection, should evince more strength and the general condition of the infant be improved. Afterward a **cool or warm compress**, 70° to 100° F. (21.1° to 37.8° C.), applied over the abdomen and covered with oiled silk and a flannel binder, soothes and assuages pain.

This **lavage of the intestines** may be repeated in six or twelve hours if deemed advisable, and perhaps afterward daily. Bowel washing, in our opinion, however, has been much overdone. With frequent large, watery movements lavage after the first day is unnecessary. Later on in the attack normal saline enemata, given in such a way as to favor absorption, are of much value in supplying sufficient fluid to the tissues, and promoting elimination by skin and kidneys.

Many physicians have advocated at this stage of the disease the administration of drugs which have some action as intestinal antiseptics. Among the more important of these drugs we may mention **resorcin, menthol, thymol, bismuth salicylate, sodium salicylate, betanaphthol**, and others. It is not to be forgotten, however, that many of these drugs are very distinct cardiac depressants and renal irritants, and may easily do more harm than good. In our opinion they are better omitted.

The following combination is highly recommended by the author in the treatment of the more severe forms of infantile diarrhea:—

℞ *Magnesii sulphatis*	ʒj-ij (4.0-8.0 Gm.).
Mucilaginis acaciæ	f℥ss (15 c.c.).
Phenylis salicyl.	gr. v-x (0.3-0.6 Gm.).
Glycerini	fʒiij (12 c.c.).
Aq. chlorof., q. s. ad......	f℥iij (90 c.c.).—M.

One teaspoonful is given every one, two, or three hours, sleeping or waking, vomiting or not. Glycerin is further added when the urine is concentrated, and a little **sweet spirit of niter** is given separately when this is very marked. In a small proportion of cases the salol disagrees, causing nausea and vomiting, and is then omitted. The character of the stools is taken as guide to the frequency of administration of the preparation. If the blood in them does not diminish, the number of doses should be increased. Continuous use of the medicine, even at night, is essential, even in children less than a month old. There should be no reduction in the doses till the "slime" has disappeared from the stools.

As regards **diet**, the author uses barley water and white of egg beaten up with an equal quantity of water, or, better, soda water. In serious cases, **peptonoids** are added, though care must be exercised in their use, as they occasionally disagree. A pinch of **pepsin** scales placed on the tongue after food is often of much benefit. H. A. Ellis (Austral. Med. Gaz., Jan. 13, 1912).

Certain intestinal antiseptics, while theoretically powerful, are too irritating to the mucosa to be used in a dose large enough to have any value. Thymol, the naphthol derivatives and phenyl salicylate, or salol, belong to this class. **Bismuth salicylate,** however, is unobjectionable. A comparison of two series of cases, one treated solely by the starvation plan and one treated with bismuth salicylate, showed such a decided difference in favor of the drug that it seemed to have undoubted disinfectant properties. Besides the direct disinfectant action of the salicylic radical there is also obtained the sedative action of bismuth itself, which may also be enhanced by giving **bismuth subnitrate** or **subcarbonate** at the same time. A. Hand (Archives of Pediatrics, Feb., 1912).

After the intestinal tract has been well cleared of offending material a sedative action on the intestinal tract may be obtained from full doses of one of the **bismuth salts.** The **carbonate** or the **subnitrate** may be given in 10-grain doses (0.65 Gm.) in an emulsion combined with small doses of an opiate and repeated every three hours till distinct improvement sets in. If vomiting is absent and the stools contain an excess of mucus, small doses of **castor oil** have in my experience proved very serviceable, especially if the pyrexia is still high.

℞ *Olei ricini* .... ʒij (8 Gm.).
Tincturæ opii camphoratæ .... ʒj-ʒiss (4-6 Gm.).
Pulveris acaciæ,
Pulveris sacchari albi,
of each .... ʒij (8 Gm.).
Aquæ cinnamomi,
q. s. ad.......... ℥iij (90 c.c.).

M. Sig.: ʒj every three hours for an infant 1 year old.

Under this treatment the pyrexia will be found to subside slowly and the frequency and character of the stools to alter for the better. The castor-oil mixture may then be replaced by **bismuth.** Later on one of the newer preparations of tannin may be added to the bismuth if the movements still continue frequent and watery. A few physicians, however, still prefer the older tannin astringents, *e.g.,* tincture of **kino** or of **catechu,** or the fluidextract of **hematoxylon.** In a few cases the tincture of **coto** has proved useful in my hands.

The value of the administration of **opium** in this disease is a subject on which there has been much difference of opinion. All writers, however, agree that it should be avoided at the onset; it should also not be employed in grave toxemic states with any tendency to drowsiness or stupor, or to cyanosis. Its administration should at once be stopped if under its use the temperature rises, and the bowel movement is unduly checked. But in the great majority of cases, if used cautiously and intelligently, no other drug is so valuable, quieting the motor and sensory systems, relieving pain, and lessening peristaltic activity, thus favoring repair. The preparation employed is immaterial, provided the dose be not too large.

For infants of 3 months:—
Tr. opii camph., ♏ij-iij (0.12-0.18 c.c.).
For infants of 6 months:—
Tr. opii camph., ♏iij-v (0.18-0.3 c.c.), or *Pulv. Doveri,* gr. ⅛-⅙ (0.008-0.01 Gm.).
For infants of from 12 months to 2 years:—
Tr. opii camph., ♏v-viij (0.3-0.48 c.c.), or *Pulv. Doveri,* gr. ⅙-¼ (0.01-0.016 Gm.).

These doses may be repeated every three or four hours, unless the child is sleeping. In apportioning the dose it is wise to consider the size and weight of the infant as well as its age.

If vomiting prevents the administration of the drug by the mouth, **mor-**

phine may be given hypodermically in $\frac{1}{100}$-grain (0.00065 Gm.) doses to an infant from 8 months to 1 year old, and repeated every six hours if necessary.

Stimulants, in our opinion, are necessary in the majority of cases; they should be used cautiously at first, but liberally in the later stages of the disease. Good **whisky** and **brandy** are preferable to wines, and of these 10 to 15 minims (0.6 to 0.9 c.c.) may be given every two hours. **Aromatic spirit of ammonia** may occasionally be of service in small, frequently repeated doses. **Caffeine** may also be employed, either in solution or in the form of a well-prepared tea or coffee. Where the prostration is severe **strychnine** in $\frac{1}{400}$- to $\frac{1}{200}$- grain (0.00015 to 0.000 Gm.) doses, given hypodermically, is of service. **Atropine,** $\frac{1}{1000}$ grain (0.000065 Gm.), hypodermically, is recommended by la Fetra. **Camphor** dissolved in oil has also proved serviceable.

In all instances where the temperature runs an elevated course we have much confidence in the value of **hydrotherapy.** This treatment may be employed in the form of tepid sponging, **cool baths,** the **cold wet pack,** or **cool irritation of the intestines.** Of the three methods our preference is for **tepid sponging** or cool baths. Whenever the temperature of the body rises above 104° F. (40° C.) the infant should be sponged with water at 85° F., or placed in a bath containing water at a temperature of 90° F. (32.2° C.), and remain in it from three to five minutes, the duration varying according to the age and feebleness of the infant. It is to be remembered that infants are affected by a cold bath more promptly than adults, and are more easily depressed by it. Care should be taken, therefore, to watch its effects, and, if necessary, to use stimulants after it is over.

A **cold pack** may occasionally, with advantage, replace the cool bath where circumstances are not convenient for the employment of the latter. Of late years the irrigation of the colon with cool **normal salt solution** has been employed in cases of hyperpyrexia. It is unquestionably a more powerful method than either bath or pack, and, when used with discretion, may prove of more value. Its action, however, is less under the control of the physician than that of baths, and serious depression of the nerve-centers may result from the employment of too cold and too long continued irrigation.

Should the prostration become extreme and hydrencephaloid symptoms make their appearance, subcutaneous injections of a sterilized **normal saline solution,** as described in the article on cholera infantum, ought to be employed. In severe cases two injections a day of 50 c.c. ($1\frac{2}{3}$ ounces) each should be given. Not only do these injections stimulate the flagging circulation, but they dilute the toxins in the blood and favor their elimination through the excretory organs; in many instances they check, in a remarkable way, the symptoms of nervous irritation.

> When the diarrhea is due to a toxemia the writer begins treatment with **castor oil,** or, if much vomiting is present, fractional doses of **calomel,** $\frac{1}{6}$ grain (0.01 Gm.) every hour until 1 grain (0.065 Gm.) is given. In mild cases boiled water given by the mouth usually rapidly cleanses the stomach by being vomited; if vomiting persists, lavage must be resorted to. Irrigation of the colon

is of advantage in every case. It should be done every twelve hours with a gallon of **normal salt solution,** at a temperature of about 100° F. (37.8° C.). **Strychnine,** 1/200 grain (0.0003 Gm.), repeated in three hours, is of advantage in the worst cases. **Hypodermoclysis,** 8 ounces (240 c.c.) of sterile salt solution, repeated in twelve hours, is also beneficial in tiding the desperate case over a critical period. High temperatures are controlled by **ice-water enemata,** 1 pint (480 c.c.) being used. **Whisky,** opium in the form of **morphine** or **paregoric,** may be given as indicated. **Subnitrate of bismuth,** in **mucilage** of **acacia** and **peppermint water,** is excellent in controlling the diarrhea.

When this is due to inflammation of the intestinal mucosa, hygienic and dietetic treatment are indicated. It is important to supervise the child's **diet** for a long while after convalescence is apparently established. **Castor oil** or **calomel** should be given in sufficient doses to sweep out the food and decomposed material thoroughly from the gastrointestinal tract. Rectal irrigation with **normal salt solution** is of benefit in almost every case. **Subnitrate** of **bismuth,** in 10-grain (0.65 Gm.) doses, every two hours, should be given continuously during the entire course of the disease. If tenesmus is present, **laudanum,** 4 drops (0.24 c.c.) in 4 ounces (120 c.c.) of starch water, may be used as an enema. Stimulants will be required in the majority of cases. **Opium** is required in all but the mildest cases. E. E. Graham (Therap. Gaz., July 15, 1906).

Careful feeding and **intestinal irrigations** with boiled water, 0.02 per cent. **boric acid** or **naphthol solution,** or, better, **normal saline solution** are indicated. The irrigations facilitate the elimination of toxic substances from the intestine and supply the loss of the body fluids caused by the diarrhea. During irrigation the child should be upon its right side; a soft-rubber catheter should be used and the receptacle of the fountain syringe through which the lavage is given should be elevated not more than five or six inches above the patient. The quantity employed should be from 1 pint to 1 quart and the fluid should be cold if the patient's temperature is elevated, hot if the latter is subnormal. As an intestinal antiseptic, 3 powders consisting each of 5 grains (0.3 Gm.) of **bismuth salicylate** and 2½ grains (0.15 Gm.) of **benzonaphthol** may be given daily. Lactic acid should not be prescribed if the patient is taking milk. If the child is less than 1 year old he may take a teaspoonful of the following mixture every half-hour: **lactic acid,** 3 parts; quince syrup, 25 parts; distilled water, 100 parts. If older than 1 year dessertspoonful doses may be given. **Bismuth**—in a mixture containing soluble bismuth phosphate, 2 parts; simple syrup, 10 parts; distilled water, 90 parts—may act well. The dose is 1 teaspoonful every hour. If vomiting is present, **gastric lavage** may be indicated. Injections of **saline solution** are often very useful. Perrot (La quinzaine thérap., vol. vi, p. 450, 1907; Amer. Jour. Med. Sci., Aug., 1907).

The treatment of diarrhea due to alimentary intoxication consists in combating the collapse, cutting short the intoxication, and slowly bringing the child back to a diet commensurate with its caloric requirements. The first indication may be met by hypodermoclysis of **saline solution,** using 50 to 100 c.c. (1⅔ to 3⅓ ounces), and repeating as is deemed necessary. The second indication is met by withdrawing the food entirely and allowing water only for twenty-four hours. With the subsidence of all symptoms, begin feeding as follows: As exceedingly small quantities of fat are injurious, begin with centrifugated breast milk, if possible, given in teaspoonful doses five times a day, or an equal quantity of **buttermilk,** to which neither sugar nor meal has been added; or, if this is not at hand, fat-free milk may be used. As a diluent, and to supply the liquid necessary, water and a thin cereal gruel may be used or given separately. After an interval of twenty-four hours, provided treatment has been well tolerated, without any evidence of return of the intoxication, the separate quantities of milk may be increased to 2 teaspoonfuls, which after two or three days may, under the circumstances mentioned, be doubled, and so on, until they are gradually brought to a **diet** (free of fat in artificially fed infants) that will temporarily meet their needs from a caloric standpoint, having added, in the mean time, with their increased tolerance of the buttermilk (where employed), 30 Gm. (1 ounce) of sugar, preferably maltose, and 15 Gm. (½ ounce) of flour to each liter (quart) of buttermilk while boiling. The child should not be kept on the buttermilk diet longer than six weeks. After this time whole-milk dilutions will be necessary to meet its needs. In case the infant was at the breast, after four or five days of careful feeding with contrifugated breast milk, it may be returned to the breast, the amount of milk being carefully controlled. Butler (Jour. Amer. Med. Assoc., April 4, 1908).

Opinion of a committee of the Academy of Medicine concerning Quinton's "marine plasma:" It consists of **sea water** collected under aseptic conditions and rendered isotonic by the addition of sterile water. It has sometimes given good results when, as the result of profuse diarrhea, the fluid content of the organism has been greatly reduced, but since ordinary physiological salt solution gives analogous results in the same case, the former cannot be considered either as a specific or panacea in infantile diarrhea. Wurtz (Bull. de l'Acad. de Méd., May 14, 1912).

Treatment of infantile gastroenteritis by subcutaneous injection of "marine plasma," *i.e.,* sterilized **sea water.** The writers give milk at once with the injections, and regard the strengthening from the milk as an integral part of the treatment; the children are transformed by the injections so that they are able to take care of the milk. Between each feeding they are given a bottle of water or it is fed to them with a spoon, giving as much water as the child will take readily. The amounts of sea water to be injected vary with the nature of the trouble. With enteritis causing constipation, they inject from 10 to 30 c.c. (⅓ to 1 ounce) twice a week, feeding the child with from one-eighth to one-sixth of its weight. With athrepsia and ordinary diarrhea, they inject from 30 to 100 c.c. (1 to 3⅓ ounces) two or three times a week, and feed from one-seventh to one-fifth of the weight. Almost moribund children recover under this regimen. They published in 1905 a series of experiments including 2592 days of tests to determine the superiority of sea water over ordinary salt solution for these injections in infants. They found that the infants increased in weight twice as fast under the sea water. This increase was not due to the weight of the sea water, as the increase in weight was out of all proportion to the amount of sea water ingested. O. Macé and R. Quinton (Revue mens. de Gynéc., d'Obstet. et de Péd., June, 1912).

Dietary.—For the first twelve or twenty-four hours, according to the severity of the case, only cool sterile water should be permitted to the infant. After this period a weak sugar-of-milk solution may be given in small quantities to infants under 3 months, and to those over 3 months thin barley or rice water with sugar of milk may be allowed. Great caution must be exercised with all albuminous foods so long as the stools retain their offensive odor. White of egg, or albumin water, forms an excellent method of administering an easily assimilated proteid. To prepare it, the white of an egg is to be shaken up in a flask with 8 ounces (240 c.c.) of water; the solution is then to be strained through muslin, and a little salt and sugar of milk added.

> Weill, Lumière, and Péhu found a 10 per cent. solution of sterilized **gelatin** in physiological saline made into a jelly and kept in a closed tube effective. Before each feeding, the solution is melted on a water bath and 10 c.c. (⅓ ounce) of it are poured into the bottle containing the milk. At the fourth or fifth stool, after the beginning of the treatment, the feces show marked improvement, the odor disappearing and the color and consistence approximating the normal. The gelatin facilitates digestion of the milk by causing the clots to break up into fine particles, and as a result the stools are rendered more solid in consistence. The measure gives especially good results in light forms of diarrhea. The necessity of stopping milk entirely may thus be avoided. Similarly, when feeding with milk is resumed, after suspending it for a time in the more pronounced cases, the use of gelatin is indicated. The writer found this treatment very useful excepting in severe diarrheas of choleraic type, gelatin having no power to counteract the infectious process. Lereboullet (Paris méd., Dec. 2, 1911).
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> **Soy flour** useful in summer diarrhea and some forms of intestinal indigestion, given in form of dilute gruel with or without addition of barley flour later, with condensed milk or cows' milk. One to 2 level tablespoonfuls of soy flour to the quart suffice at first; later increased to 4 spoonfuls. Soy-bean, barley, and condensed-milk mixtures are useful where, cows' milk disagreeing, there is difficulty in finding food sufficiently nutritious for child. Orange juice is advisable from time to time to prevent tendency to scurvy. Ruhräh (Archives of Pediatrics, Oct., 1911).

A carefully prepared whey may also be allowed, and is often relished. In older children a weak broth with barley or rice, or one of the peptonized foods may be administered with advantage. Milk in all forms should be forbidden in the early acute stage; only when the pyrexia has, in great measure, subsided, and the stools have begun to assume a more normal appearance, may a weak dilution of a comparatively fat-free milk be allowed; the strength of this dilution should be only gradually increased.

> As soon as the diarrhea begins, **castor oil** should be administered and food should be withheld for at least twelve hours. During this period water should be given frequently, by mouth if there is no vomiting, by rectum if vomiting is present. The best treatment for the vomiting is **lavage** and **starvation.** If the infant presents symptoms of marked loss of fluid, such as a dry, loose skin, parched tongue, depressed fontanel, and sunken eyes, **salt** should be added to the water, so that a **hypotonic solution** of 0.3 or 0.4 per cent. is given. If we make use of a normal solution edema is apt to ensue. Fever should be controlled by means of occasional **baths** at 85° F. (29.4° C.) and frequent **packs** at this temperature or lower, if necessary. There is no medicine, except, perhaps, a stimulant in case of collapse or severe prostration, which has any value; bismuth, the astringents, and the opiates are ineffectual. One of the fundamental principles of the **feeding** is that it should be begun in very small quantities, a teaspoonful every two or three hours. Another rule is that fats and sugars should be avoided. We must not forget, however, that the various food constituents differ in their action according to their correlation. For example, sugars when given with dextrin or starches lose their laxative effect. The same is true for both fats and sugars in combination with proteids. It is due to these considerations that we can

begin with the feeding of the "**casein milk**" of Finkelstein, a food containing a high percentage of proteid, a moderate amount of fat, and but little sugar and salt. If we have not this food at our disposal, skimmed milk may be given in small doses. Hess (Jour. Amer. Med. Assoc., July 15, 1911).

Underfed, poorly nourished infants with diarrhea, do best on the **milk and water** mixture, boiled, without sugar. Bad diarrheas, or those that do not improve upon these mixtures are benefited by **albumin milk.** Infants that have had repeated or prolonged attacks of diarrheas do best upon *Eiweiss Milch.* Older, well-nourished infants with a diarrhea do best upon a **barley-gruel diet** for a few days. Infectious diarrhea, if seen early, should have a **cathartic** and **starvation** for forty-eight hours and no longer. The milk-and-water mixtures, boiled, or *Eiweiss Milch* **(albumin milk)** should then be given. Cathartics should be given to infants with diarrhea with great discretion. Dennett (Med. Rec., Dec. 2, 1911).

Report of results obtained in summer diarrhea with **albumin milk** according to Finkelstein and Meyer. This is prepared as follows: A tablespoonful of essence of rennet (or 2 tablets of rennet) is added to 1 liter (quart) of milk, which is then placed in a water bath at 42° C. (107.6° F.) for one-half hour. It is then filtered slowly by gravity without any pressure for about an hour, through cheesecloth. The coagulum is then washed twice in half a liter (1 pint) of water through a very fine sieve and forced through by means of a wooden club. Then half a liter (1 pint) of buttermilk is added. This mixture was given for from two to fourteen days, in quantities corresponding to the usual feeding mixtures prescribed for the respective age. In the series of 42 cases, 20 of which belonged to a very severe type of the disease, there were 9 deaths, a mortality of 21 per cent. Excluding 4 of the cases in which the children were practically moribund when admitted, there were 5 deaths, a mortality of 13 per cent. The special indication for this mixture is found in those cases in which marked emaciation has taken place owing to undue prolongation of restricted diet. Heiman (Amer. Jour. of Obstet., Aug., 1912).

The writer used **casein** or **albumin milk** in 175 cases of gastroenteritis in infants. Of these 110 were dyspepsia, 8 toxic enterocatarrh, 40 enterocolitis, and 17 decomposition (Finkelstein nomenclature). There were only 12 deaths among all these cases, which could not have been averted with any other feeding. Four of these patients were brought into the hospital moribund and 4 had bronchopneumonia; of the other 4 deaths 1 was a case of toxic enterocatarrh, and 3 were very severe decomposition. According to the writer's observations fourteen days of casein feeding suffices in most cases (Finkelstein and Meyer recommend from six to ten weeks). Casein milk offers the best method of treatment of diarrhea in infants. Beck (Jahrbuch f. Kinderheilkunde, March, 1912).

Notwithstanding the extreme heat of 1911, the epidemic of summer diarrhea was comparatively benign, only 100 of the infants dying during the month of August, although there were over 3000 sick. The writer had in the hospital 58 exceptionally severe cases, but only 6 of the infants died, a mortality of 10 per cent. This favorable outcome was due to his method of feeding the infants. Nothing but water was allowed until the alarming symptoms had subsided, the coma, collapse, high fever and albuminuria; this generally took from one to three days. Then he gave the infant the ordinary milk mixture, but without the usual 2 per cent. of cane-sugar, diluting the milk with 4 parts water, then with 3 parts, and then 2 parts. This was generally borne by the end of the first day, and he kept this up until all signs of intoxication had disappeared and the infant was ready to drink spontaneously. Then he returned to the sugar, 1 part milk to 2 parts barley water. The diluted milk without sugar seemed to answer the same purpose as "albumin milk" of Finkelstein and Meyer. C. E. Bloch (Ugeskrift f. Laeger, July 4, 1912).

During the past few years the value of **buttermilk**, either raw or pasteurized, has been emphasized by many clinicians. Buttermilk contains very little fat, a moderate amount of sugar, and a considerable amount of digestible proteid in the form of lactate of casein. It is distinctly acid, owing to the presence of lactic acid, and in the raw state is swarming with lactic acid bacteria. The lactic acid and the lactic acid bacteria have an inhibiting action on the development of other forms of bacteria.

No better basis for an artificial food for children in the first year of life exists than **buttermilk**; further, in cases of gastrointestinal disorders in infants, with the passage of fluid, partially digested stools, its use as a **diet** is attended in most cases with excellent results. Frequently within two or three days the diarrhea ceases, firm normal stools are passed, and the child begins to increase in weight. It is important that the buttermilk should be derived from the cream of perfectly fresh whole milk. A food prepared by adding 1 ounce (30 Gm.) of wheaten flour and 1½ ounces (45 Gm.) of cane-sugar to every 2 pints (1 liter) of buttermilk, the whole being boiled, with stirring, for two minutes, recommended. Quantities varying from ½ pint (¼ liter) to 2 pints (1 liter) were given daily, and although the children did not like it at first they soon took it well. In a few cases it was found unsuitable and a more fatty diet resorted to. The infant mortality in the Kaiser and Kaiserin Friedrich Hospital in Berlin has fallen since the use of this food. The good results are due chiefly to the presence of the casein in a finely divided form, and the writer does not think the diminished fat content of great importance, though most writers consider this factor also of value to feeble digestion. Caro (Arch. f. Kinderheilk., Sept., 1902).

Infants with severe gastrointestinal troubles improved to a remarkable extent when put on **buttermilk.** In 22 cases of acute gastroenteritis, including 8 very severe ones, all the children recovered rapidly, as also 3 adults with mucomembranous enterocolitis and a large number of children with chronic gastrointestinal troubles. The toxi-infectious symptoms vanished in the acute cases in less than twenty-four hours. Decherf (Semaine méd., vol. xxiv, No. 44, 1904).

All infants do not do equally well with the same nourishment. Even under the same mixture of cows' milk, it often happens that one child will do very well, while another will be very constipated, and still another infant will have very loose stools. The reason for this is explained by the congenital variance of different infants. Constipation in infants can usually be cured by the addition of one or two carbohydrates. Diarrhea, on the other hand, is more difficult to cure. The writer used **buttermilk** in cases of diarrhea with very good results. It contained about 1.4 to 1.7 per cent. of fat. Instead of adding sugars to the buttermilk, he added flour, about 50 Gm. (1⅔ ounces) to the quart (liter). This buttermilk differs from that commonly used in having a higher proportion of fat and also in having very little sugar, which, it is well known, causes diarrhea. In mild cases of diarrhea substituting this buttermilk feeding for one or two of the regular feedings often has the desired result. Karl Stotte (Monats. f. Kinderheilkunde, June, 1912).

In most instances the infant is apt to object to its taste, but this is improved by the addition of a cereal gruel and 5 grains (0.3 Gm.) of cane-sugar to the ounce of buttermilk. The whole may then be pasteurized, if desired. Morse states that he has obtained better results in the treatment of diarrheal cases from pasteurized buttermilk than from any other milk preparation.

The use of the **lactic acid bacillus,** chief among which is the *Bacillus bulgaricus,* has also been praised by various writers.

> The writer advises that the clear fluid from Bulgarian buttermilk be used as the culture medium for injection. The following are his directions: Take 500 c.c. (1 pint) of pure milk, remove the cream, add 10 Gm. 2½ drams) of cane-sugar, and boil for a quarter of an hour; cool to 42° C. (107.6° F.) and add 1 tablet of the **lactobacilli,** crushed. Keep for ten hours in a water bath at 42° C. (107.6° F.), when the buttermilk will be formed thick and creamy. Place in a refrigerator until a fluid separates, and siphon off the clear fluid from the bottom. This fluid is rich in bacilli, sugar, and peptones, and is ready for use in the manner suggested. Even though further trials prove its efficacy, the trouble involved in its preparation will be a serious deterrent to its use in private practice, although there should be no difficulty at institutions with a bacteriological laboratory. W. H. Walsh (The Hospital, Dec. 5, 1908).
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> The bacterial diarrheas of infants may be classified into parasitic and saprophytic, the former of which must be combated by serotherapy and vaccine while the latter require other methods, one of which is specially taken up by the writer, namely, the antagonism of the lactic acid bacteria to the fermentation conditions in the intestine. His investigations on this subject were prompted by the work of Tissier in the Pasteur Institute in Paris, who found that the predominating organism in the healthy infantile intestine is *Bacillus bifidus,* while in disease other forms appear. Among these latter Tissier found only one, *B. perfringens,* that was pathogenic to animals, which attacks protein substances and their derivatives. It is a large rod with square ends, staining by Gram's method; is anaërobic, ferments sugar and has the special property of causing solution of meat or the white of egg in sealed tubes. Tissier believes this organism to be the cause of fermental diarrhea. As predisposing causes, he believes that lack of digestive power and unsuitable food play the chief part. The indications for treatment he thinks are removing the fermenting intestinal contents by purgation and restoring the normal intestinal flora. The increase of carbohydrates in the food will favor the latter, but the more specific treatment is to introduce into the intestines an organism capable of inhibiting the growth of the abnormal forms, which he found most conveniently in the lactic acid bacillus. Taking up these ideas of Tissier, the writer began his work on the subject in the autumn of 1905 and has continued it since then. **Buttermilk,** containing large numbers of lactic acid bacilli, seemed to him to combine both food and medicine. The selected buttermilk was first pasteurized to kill all other organisms and then inoculated with a pure culture of lactic acid bacilli and ripened until the development of the organism had brought about the proper acidity and precipitation of the casein. In the majority of cases the buttermilk was used only after other measures had failed. After a dose of **castor oil** or **calomel** to empty the bowel nothing but boiled water was given for twenty-four hours and only barley water for another twenty-four, then a weak milk modification was used, gradually strengthened as improvement appeared. In the first 35 cases tried with the **lactic acid** treatment, 5 were not strictly fermental cases, but were selected for experiment, and in these no improvement was seen. In 23 there was a rapid change in the character of the dejecta

and gain in weight. In 3 cases the diarrhea ceased without gain in weight and in 9, including those mentioned above, there was no improvement. Only 2 of the cases of total failure were frankly fermental cases, 2 were dysenteric. The use of non-pasteurized buttermilk was tried in 14 resistant cases after pasteurized milk had failed, and in these cases immediate improvement followed its use, which he attributes to the introduction of large numbers of living lactic acid bacilli into the intestine. The results were so favorable that he concluded to adopt this treatment as a routine, and he has thus treated several hundred cases of which he has fairly complete records of 120. Not all of the babies received unpasteurized buttermilk; some were treated with various formulas of modified milk similarly ripened. In all of these that were truly fermental diarrheas, numbering 100, the treatment was successful in 74, partly successful in 12, and failed in 14. There are occasionally cases in which buttermilk does not seem adapted to the child's digestion, and these were treated by only continuing it until the alteration of the movements had occurred, as a temporary weapon against the saprophytic infection. The attempt to use modified milk, similarly ripened, was not a complete success, and he was compelled to confine his work to formulas containing no fat. There is also a difference in the effects of different strains of lactic acid bacilli, and he is still experimenting as to this point. His general conclusion is, however, that in this treatment we have a very valuable weapon for combating fermental conditions, and that it should be used in every case of this type. C. H. Dunn (Jour. Amer. Med. Assoc., Aug. 21, 1909).

Bacillus bulgaricus was used by the writer with marked benefit, all cases except the most advanced being cured. After preliminary dose or two of castor oil, liquid cultures were given in doses of ½ or 1 teaspoonful every three or six hours, in a little water with milk-sugar. **Diet** for first one or two days: Whey from pure milk, diluted according to age; later, add milk in increasing amount, and for older babies barley or other cereal water. Milk used must be free of preservative, otherwise lactic bacilli inhibited. Where purity of milk not certainly known, give barley water with lime water and milk-sugar, and later add condensed milk. In breast-fed infants, milk usually continued and cultures given between feedings. Harrington (N. Y. State Jour. of Med., Feb., 1912).

Hygiene.—During the attack the infant should, as far as possible, be confined to its cot. Soft, unirritating flannel should be worn over the abdomen to afford some protection against sudden changes of temperature in the external air. Great care should be exercised lest the buttocks become irritated by the discharges; diapers should be changed promptly as soon as soiled, and the application of some greasy emollient will frequently prevent the development of the erythematous and sometimes ulcerative condition which in these cases is so liable to occur.

The infant, of course, should be allowed all the fresh air possible. The room in which the infant is kept should be light and well ventilated, and an effort should be made to maintain its temperature between 65° and 68° F. This in midsummer in cities is well-nigh impossible. But sometimes much can be done by keeping the patient on the shaded side of a veranda or in a tent on a lawn. Electric fans keep the air moving and encourage evaporation on days extremely oppressive. As soon as the violence of the attack has passed off, the infant should be sent, if practicable, either to the seaside or to a bracing country or mountain air.

INFLAMMATORY DIARRHEA in which, in Addition to the Systemic Infection, the Symptoms of an Acute Local Inflammation Have a Prominent Part—ACUTE ILEOCOLITIS. DYSENTERY.

Under the term ileocolitis, or dysentery, several forms of inflammatory diarrhea have been described. In the cases most frequently met with the symptoms are chiefly catarrhal; in a few the intensity of the inflammation leads to a necrosis of the superficial tissues and the formation of a pseudomembrane, and in a third class an ulceration of the lymph-nodes and tissues surrounding them is the chief characteristic. These divisions, however, are more easily made by the pathologist than by the clinician, although in typical cases the symptoms may point strongly to one or other form.

Inflammatory diarrhea is more frequently met with in the later than during the earlier weeks of summer, and may occasionally appear as a limited epidemic. For the special ætiology and morbid anatomy we must refer the reader to what we have already said at the beginning of this article.

> The mere presence of a few dysentery organisms in a case of acute intestinal disturbance in an infant does not in itself prove that the organisms have any etiologic relation to the condition. It is only in the severe cases of ileocolitis that the dysentery organisms are present in the stools as one of the predominating types of organisms, and it is these cases which show distinctive lesions of dysentery at autopsy. In only about 20 per cent. of the cases of ileocolitis occurring in infancy are dysentery organisms found. While in some of these cases the infection with dysentery organisms is primary, in others it is probably secondary. The cases of ileocolitis in which dysentery organisms are present cannot be separated clinically from those in which they are absent. Streptococci are present in the stools of about 80 per cent. of the cases of ileocolitis. B. S. Veeder, R. Kilduffe, and O. T. Denny (Amer. Jour. of Dis. of Children, Aug., 1912).

Symptoms.—The symptoms in this form of the disease generally commence abruptly, and for the first few days closely resemble those of the preceding form. The vomiting, however, is not so persistent; the temperature, although high at the onset, soon falls, and remains about 103° F., and the motions are fluid, of a greenish or greenish-yellow color, and frequent, gradually becoming less in amount. They are passed with considerable abdominal pain and rectal straining, and contain much mucus and a variable amount of blood. Their color changes to brown or greenish-brown, and their odor becomes offensive. Under the microscope undigested material, epithelial cells, pus-corpuscles, and streptococci, with other forms of bacteria, are seen.

The abdomen may show signs of distention; tenderness on pressure may be elicited along the course of the colon, and the urine, if collected, may show the presence of a small amount of albumin. As the disease progresses the severe straining frequently leads to a troublesome prolapse of the bowel.

If proper measures are employed, the severity of the symptoms generally subsides toward the end of the first week. The motions diminish in frequency; they no longer show signs of blood; pain and tenesmus lessen, and the mucus decreases in amount. Recovery, however, is apt to be slow, and, for some time, relapses on the slightest indiscretion are liable to take place. The persistence for several weeks of brown mucous stools, with moderate pyrexia and a failing nutrition, are, according to Holt, an indication that ulceration has taken place. In the more severe form the temperature remains steadily high; the motions are very frequent and contain much blood, and the infant quickly falls into a typhoidal state, in which stupor, delirium, or convulsions are liable to occur. If the case survive, the symptoms may moderate; but prostration is extreme, and some pulmonary or cerebral complication is apt to turn the scale on the wrong side. More or less ulceration is always present in these cases, rendering recovery particularly slow. A long period, during which careful dietetic and medicinal measures must be faithfully employed, is required before complete restoration to health can be secured.

The membranous type of the disease is, fortunately, of rare occurrence. In this form the symptoms are of an alarming character from the very outset. Not only do the stools contain much blood and mucus, but an examination of them under water may reveal numerous shreds and sometimes large patches of pseudomembrane. Pronounced nervous symptoms, such as stupor or convulsions, may at the onset mask the symptoms of local inflammation. Such cases generally run a severe course, typhoidal symptoms develop early, and recovery is comparatively rare.

Occasionally we meet with cases which, for the first two or three weeks, have shown symptoms of gastroenteric infection rather than of local inflammation, and in which, owing to the feeble constitution of the infant and to the intensity of the local irritation, a follicular ulceration develops and symptoms of local inflammation make their appearance. The motions become slimy and show traces of blood; their color is, most frequently, a dark green or brown, and their odor offensive. Pain at this stage, though present, is no longer so prominent a feature as during the earlier stages of the disease; pyrexia is only moderate; the motions are not very frequent, but the strength of the infant gradually fails, and general emaciation becomes very noticeable. Under the microscope the stools are seen to contain epithelial cells in large numbers, numerous leucocytes, and streptococci associated with bacilli.

The course of these cases is generally downward. The disease assumes a chronic character. Exacerbations and relapses are easily excited. Only the few recover completely, and in these convalescence is always slow. The fatal result is frequently hastened by some intercurrent disease.

Diagnosis.—Great care must be taken to differentiate this form of diarrhea from intussusception, as in the case of the latter disease much valuable time may be lost. In the early stages of intussusception we have no pyrexia. Vomiting is an initial symptom, and is followed by recurring colicky pains with straining. This group of symptoms should always put us on our guard, especially if blood-stained mucus is passed almost free from fecal matter. Careful palpation of the abdomen should be made to elicit any signs of tumor. Should any rigidity of the abdominal wall interfere with effective palpation, it is often advisable to procure complete relaxation by means of a little chloroform. Typhoid fever, as we have before mentioned, very rarely presents itself in an infant. Severe membranous diarrhea may be confounded with meningitis at the onset, but the course of the disease will make the diagnosis easy.

A careful study of the autopsy records and clinical histories of 100 fatal cases of infantile diarrhea occurring in a series of years at the Thomas Wilson Sanitarium, Baltimore, brought out the following facts: "1. Mucus is evident to the naked eye in a large percentage of diarrheal stools of infancy. Its absence renders the presence of serious intestinal lesion improbable. Mucus in large amounts may be found in the stools in all intestinal disorders, but the proportion of cases with extensive intestinal alteration is greater when the quantity of mucus is in considerable excess. 2. The appearance of blood in the diarrheal dejecta of infants suggests an alteration of the intestinal mucosa in proportion to the amount of blood present. On the other hand, extensive changes may occur in the bowel wall without the macroscopic presence of blood in the discharges. 3. In like manner, the presence of pus in the diarrheal stools of infants indicates, according to its quantity, alteration in the mucosa, particularly that of the large bowel. The failure, however, to detect pus in the stools with the naked eye does not preclude the possibility of extensive intestinal lesion. 4. Blood and pus are more frequently found in diarrheal movements in the middle half of infancy, and these elements at this time form a correspondingly more reliable index of the conditions of the intestinal mucosa. 5. Blood and pus rarely appear in the diarrheal discharges of infants before the beginning of the second week of their illness. They are more frequently found from the third to the sixth or eighth week, and are usually absent after this period, when, if the baby survives, the condition may assume a marantic character. 6. Blood and pus are often found mingled in the same stool. Less often blood appears alone, and still less frequently is pus noted in the dejecta of infants who have not passed blood. The presence of these elements indicates the probability of thickening and infiltration or of ulceration of the mucosa of the small, but more certainly of the large intestine." J. H. M. Knox (Jour. Amer. Med. Assoc., Oct. 17, 1908).

A diagnosis of the presence of ulceration is to be made from the whole character of the case and its history, rather than from any one special symptom. When mucous stools persist for several weeks with only moderate fever, but with rapid wasting and loss of strength, a condition of ulceration is more than probable.

Case of ileocolitis in a boy of 3 years complicated by the presence of tapeworm. The boy was taken violently ill with all the symptoms of ileocolitis, which persisted for about three days, then gradually subsided, the treatment having consisted of colonic irrigations and a carefully regulated diet. Ten days later sections of the *Tænia saginata* were found in the stools, and later the boy again became violently ill. Being in an extremely weakened condition measures were employed to build him up as rapidly as possible. Tonics were used, good substantial food given, and the seashore recommended. Four attempts were made at various intervals for the removal of the tapeworm, the entire worm being finally passed ten months after its discovery. M. Ostheimer and H. A. Spangler (Penna. Med. Jour., Sept., 1908).

Prognosis.—The prognosis must be greatly dependent on the vitality and strength of the infant, upon the hygienic and dietetic conditions that can be secured, upon the severity of the attack, and upon the season of the year. Delicate infants under unhygienic conditions generally succumb early. Continuous high fever, the presence of a large amount of blood in the evacuations, severe nervous disturbance, and symptoms indicative of extreme feebleness of the circulation are always to be regarded as unfavorable.

Treatment.—The same measures are to be employed at the outset in this group of cases as in the preceding. Milk and all milk foods are to be forbidden. A full dose of **castor oil** or an effective dose of **calomel** is to be promptly administered, and followed within a few hours by copious irrigations of the colon with tepid **normal saline solution.** A **compress over the stomach,** to which we have already referred, should be applied. After complete irrigation of the intestines, should painful straining persist, a small quantity (ʒj to ʒij—4 to 8 Gm.) of a thin **starch solution,** to which from 1 to 3 drops (0.06 to 0.18 c.c.) of **tincture of opium,** according to the age of the infant, has been added, should be gently thrown into the rectum, with the object of moderating excessive peristalsis and lessening tenesmus. These opiate injections may be repeated every four hours, watching their effects carefully. Should the stools contain a large amount of blood, rectal injections of **hot normal saline solution,** 106° F. (41.1° C.), to which a small amount (ʒj to ʒij to Oj—4 to 8 c.c. to 30 c.c.) of solution of **adrenalin,** 1 to 1000, has been added, may be slowly administered, allowing the fluid to escape without hindrance. Fluidextract of **hamamelis** (ʒiv to Oj—16 to 30 c.c.), **tannic acid** (gr. xxx to lx to Oj—2 to 4 c.c. to 30 c.c.), and weak **nitrate of silver** (1:2000) solutions have all been recommended for use in this acute stage. We consider them of more advantage after the acute symptoms have subsided.

Yeast has been found a very satisfactory remedy in various cases of gastrointestinal affections in children at the Strassburg polyclinic. The benefit was particularly striking in enteritis accompanied by much putrefaction in the intestines. The yeast preparations alone triumphed in several very severe cases that had not responded favorably to calomel, bismuth, or lavage of the intestines. In other cases the ordinary measures seemed to do no good until reinforced by the yeast. Sittler (Münch. med. Woch., Bd. liii, Nu. 36, 1906).

Internally, during the acute stage, we place most reliance on an emulsion containing **castor oil,** in from 3- to 5-minim (0.18 to 0.3 c.c.) doses, associated with **Dover's powder** or **paregoric** (*vide* treatment gastroenteritis), and given at intervals of three or four hours. This emulsion should be made palatable. After the acute symptoms subside, one of the insoluble preparations of **bismuth,** to which we have before referred, should be given in full doses, suspended in a mucilage with some aromatic water. More powerful astringents are only permissible in the later stages. **Opium** in doses sufficient to relieve pain and restlessness is, in our opinion, of distinct service. Stimulants are required in the majority of cases. Old **brandy** or **whisky** forms one of the best, and, given well diluted in a little sweetened or albumin water, is acceptable even to the youngest infant.

This mixture is useful when dietary restrictions are unnecessary:—

℞. *Gambir* (*catechu*)	2.0	Gm. (30 grains).
Tincturæ cinnamomi ...	10.0	Gm. (2½ drams).
Benzosulphinidi ..	0.925	Gm. (15 grains).
Aquæ destillatæ ...	90.0	Gm. (3 ounces).

M. Sig.: One teaspoonful every half hour. R. Fischl (Nouveaux Remèdes, June 24, 1912).

All that we have said in the preceding section in reference to **cool baths, dietary**, and general hygiene is equally applicable to this class of cases.

> The writer advocates the use of alkalinized **kefir**. To ½ a liter (1 pint) of kefir he adds ½ a liter (1 pint) water and 5 c.c. (80 minims) of a 20 per cent. solution of **sodium carbonate**. The sugar content of the mixture is about 1.5 per cent.; albumin 1.0 per cent., and fat 1.7 per cent. It checks fermentation and brings about a normal condition of the stools. Its use should not be continued long after the stools return to normal, as it is not sufficient for the child's proper nourishment. It is easy to prepare, and it is cheap and therefore adapted for use in clinics. J. Peiser (Monats. f. Kinderheilkunde, Bd. xi, Nu. 5, 1912).

CHRONIC DIARRHEA.

Etiology.—The chronic form of diarrhea is met with as the result of a previous acute attack or arises in an insidious manner from prolonged irritation of the intestinal canal by ill-digested and more or less fermenting food.

In those cases in which it is the result of an acute attack we have, as a rule, to deal with definite organic lesions. In some the persistent irritation is due to an ulceration of the intestinal wall, generally follicular, but occasionally catarrhal in character. In others we meet with an atrophic condition of the tubular glands and villi in the small intestines, associated with marked cell proliferations in the adenoid tissue of the mucosa (Holt). In a few instances the constitution of the infant has been so profoundly impaired by the acute attack that the various systemic functions are re-established with difficulty. Digestion continues to be imperfectly performed, and fermentation with the development of irritating and toxic products takes place, leading to a continued systemic intoxication, which manifests itself in anemia, defective general nutrition, and an irritable nervous system, and is associated with persistent looseness of the bowels.

Symptoms.—Cases of chronic diarrhea form a considerable proportion of the diarrheas met with during the autumn. In the first class of cases the symptoms of acute inflammation have, to a great extent, subsided; the temperature remains, for the greater portion of the day, normal, and sometimes falls even below the normal line; pain and tenderness have almost entirely passed away, but the motions still remain too frequent; their odor is offensive, blood is occasionally seen in the form of minute dark specks, and mucus of a greenish or brownish color is still present in considerable amount. The consistence and color of the stools are variable. At one time they are of nearly normal consistence and fairly homogeneous; at other times they are quite fluid and associated with much flatulence. Prolapse of the bowel occurs only occasionally.

The appetite is very variable; vomiting may occasionally occur; but a fair amount of nourishment is generally taken during the twenty-four hours. Nevertheless, the infant remains pale and weak, and lies in a helpless and apathetic manner. As the disease progresses nutrition steadily fails, and weight is lost, chiefly through wasting of the subcutaneous tissues, so that the inelastic skin hangs in folds over the shrunken limbs. In many cases the abdomen may be distended, but in others it is soft and retracted. Palpation generally reveals the liver and spleen to be of normal size. The mesenteric glands through the abdominal walls can rarely be felt, although in post-mortem examinations they are generally found to be enlarged. Petechial spots occasionally are seen on the abdomen and on the extremities. The circulation is very feeble. The lower limbs are always cold, sometimes cyanotic, and occasionally edematous. The urine is scanty. The nervous system suffers with the general failure in nutrition. The infant is peevish, easily disturbed, and sleeps badly at night.

The progress of these cases is by no means uniform. Some weeks may show a slight gain; but trivial causes, a chill to the surface of the body or a slight irregularity in feeding, may bring on a relapse, in which the gain is usually soon lost.

Complications are apt to arise. Thrush is not uncommon. The frequency of a latent otitis must always be remembered. Bronchitis is liable to appear and may develop into a pneumonia. Occasionally we meet with a general adenitis or a still more distressing furunculosis. Only rarely is nephritis encountered.

While a fatal termination occurs in a large percentage of these cases, in a few under careful dietetic and hygienic treatment the appetite gradually returns, the stools become more normal, nutrition gradually improves, and in time convalescence is thoroughly established.

In a second class of cases chronic diarrhea establishes itself without any preceding acute attack. Eustace Smith considers that in a considerable number the affection is due to repeated chillings of the surface of the body, producing a catarrhal condition of the gastrointestinal tract.

A faulty dietary is at all times an important factor, especially when associated with the depressing influence of unhygienic surroundings. This form of diarrhea is frequently met with in foundling institutions and hospitals.

The onset of the attack is gradual and insidious. A failure to gain in weight or an actual loss may be the first symptom demanding attention. The evacuations will be found to be more frequent than normal, unduly large in amount, pale in color, and pasty in consistence. As the disease progresses the stools become quite frequent, at times frothy and sour-smelling, at other times thin, dark-colored, and offensive. The abdomen is distended. A cool perspiration occurs when the infant falls asleep. The urine becomes scanty and contains both indican and urobilin. The skin assumes an earthy hue, and the face acquires a curious look of old age. The infant lies in its cot in a helpless apathetic state, and makes its wants known by a scarcely audible whine. Such infants readily succumb to some intercurrent disease. Any of the complications which we have already referred to in connection with the preceding group may be met with in this condition. The mortality is very great.

Diagnosis.—It is often difficult in these cases to decide whether the condition present in the intestine is a sufficient explanation in itself of the serious failure in general nutrition, or whether we have, in addition, to deal with some underlying constitutional disease. The question will always be a difficult one, but the physician will act wisely if he bases his opinion upon the history of the case and the general condition of the patient rather than upon any one particular symptom or physical sign.

Prognosis.—The prognosis in cases of chronic diarrhea must always be very guarded. To some extent it is dependent upon the previous constitution of the infant, on the hygienic conditions obtainable, and upon the zeal and regularity with which all instructions are carried out. When ulceration is present to any considerable degree, the prognosis is always bad, although, under favorable conditions, not hopeless. In determining its existence our chief dependence must be placed on the previous history. The longer the inflammation has lasted and the higher has been the temperature, the greater the probability of ulcerative lesions (Holt).

Treatment.—With the conditions present in chronic diarrhea no good, but often harm, may result from the employment of ordinary astringent, or even antiseptic, remedies administered by the mouth. If drugs are to be given only those should be employed which will not disturb the stomach, and may, to some extent, improve general nutrition. Some cases among older infants do, undoubtedly, derive benefit from the prolonged administration of **iron.** It may be given in one of its acid preparations or in a neutral and less irritating salt. Nutrition may, to a small extent, be assisted by the inunction over the abdomen, or body generally, of codliver oil or cocoa butter. The moderate employment of stimulants is called for in almost all cases. Great attention must be given to the proper regulation of the **dietary**; to this end the stools should be frequently examined. Fats should be eliminated completely until distinct improvement sets in, and then only permitted in small amounts. Milk must be fat free.

Buttermilk, as recommended in the acute form of diarrhea, has, in my hands, often proved of value. Starchy foods should be more or less predigested. Considerable benefit may be derived from the employment of scraped meat, meat juice, broths, and peptonized meat foods. No absolute rules can be laid down suitable for all cases, but each case must be studied by itself.

We have before insisted upon the necessity of placing the patient under the most perfect hygienic conditions attainable, and especially of securing an abundance of **fresh air.** In the treatment of those cases which are deemed to be dependent upon ulcerative conditions our chief therapeutic reliance must be placed on the careful use of astringent injections into the colon. Weak solutions of **silver nitrate** (1:2000 to 1:1000), or one of the **salts of zinc** (1:500 to 1:250), or of **tannic acid** (1:100), or of the fluidextract of **hamamelis** (ʒiv to Oj—16 to 30 c.c.), or the colorless fluidextract of **hydrastis** (ʒij to Oj—8 to 30 c.c.) may prove of value. These injections should only be used after thorough irrigation of the bowel by **normal saline solution,** and to be of service should reach at least all the descending colon. This method of treatment may easily be overdone. Their too frequent employment has often appeared to depress the infant and to irritate the intestinal mucosa. Warm **injections of** thin **starch water** or of **gelatin** have, on the contrary, often a very soothing effect.

Opium should be made use of only to moderate excessive peristalsis, and in these cases it is best given in a little **starch water** by **rectal injection.** (For Cholera Infantum see Vol. III.)

A. D. Blackader
and
William Francis,
Montreal.

DIAZO-REACTION.—Ehrlich discovered that in certain pathological conditions the urine gave a deep-red color when treated with diazo-compounds and ammonia. This has been called the diazo-reaction which normal urine never gives.

> Von Jaksch (Clinical Diagnosis, 1897, p. 375) believes the reaction to be due to acetone. "Spath claims that the reaction should be ascribed to oxyproteic (uroproteic) acid, a recently discovered normal urinary constituent, in case the urine contained an increased quantity of this substance." (Diagnostic Methods, Sahli, 1909). Sahli attributes the reaction to a pathological decomposition of the proteids. Todd (Clinical Diagnosis, 1912) attributes the presence of acetone bodies in the urine to "some obscure metabolic disturbance resulting from digestion of fats." Clinical evidence does not show the reaction to be due to acetone or uroproteic acid, but shows rather that the reaction is due to an allied substance resulting from diseased metabolism, or, which is less probable, an overproduction of the named constituents occurring in sufficient quantities to give the test only in diseased conditions. C. S. Vivian (Med. Rev. of Reviews, Dec., 1912).

Two solutions are necessary:—

Solution "A" consists of

Sulphanilic acid....	5 Gm. (1¼ drams).
Concentrated hydrochloric acid	50 c.c. (1⅔ ounces).
Water	1000 c.c. (1 quart).

Solution "B" consists of a ½ per cent. aqueous solution of sodium nitrite.

TEST.—Fifty parts of solution "A" and 1 part of solution "B" are thoroughly mixed in a clean test-tube. To this is added an equal volume of urine, and the mixture is well shaken. A few drops of strong ammonia are allowed to run down the side of the test-tube. If the reaction is positive a red ring will be produced at the line of contact of the first mixture and the ammonia. Upon shaking, the whole solution assumes a bright-red color, the same color being imparted to the foam. If allowed to stand about twenty-four hours a green precipitate forms at the bottom of the tube. Ehrlich regards this as an especial characteristic of the true diazo-reaction, although it is not always present.

Normal urine gives an orange color when treated with the above solutions. Sometimes the urine assumes a yellow color before the addition of the ammonia, upon the addition of which it becomes a lighter yellow. This Ehrlich calls the "egg-yellow reaction," and is supposed to be due to the presence of urobilinogen. This reaction is supposed to be especially indicative of the approaching crisis in pneumonia. If there is an excess of biliary pigment in the urine a dark discoloration may occur which becomes, upon boiling, a reddish-violet color.

> New method of performing the diazo-reaction of Ehrlich. The writer employs paranitrodiazobenzol sulphate, known in commercial chemistry as azophorrot P. N. The test is performed in the following manner: A few granules of azophorrot P. N. are placed in a test-tube with water (tap water may be used). The tube is inverted once or twice. Enough of the reagent is thus dissolved in the cold for use in the test. The urine is treated carefully with potassium or sodium hydrate (not with ammonia) until a slight turbidity remains. The aqueous solution of azophorrot P. N. is then added. If a bright-red color appears and, after shaking, the foam is red, the reaction is positive. With an intense reaction the color is cherry red. In a large series of cases tested with this method and the original technique of Ehrlich, the results corresponded invariably. The advantages of the new method are: the substitution of a dry substance for the two solutions, there is no necessity for accurate mixing of the reagents, and the technique is much simpler. K. Feri (Wiener klin. Woch., Bd. xxv, S. 919, 1912).

Certain drugs, chrysarobin, opium, and the phenol derivatives, cause the urine to give an apparently positive diazo-reaction, which is not the true reaction. According to Wood the foam is more of a yellow color than in the true diazo; the green precipitate never forms upon standing; the color is more permanent in the diazo, and does not fade upon the addition of a strong mineral acid. Burghart observed that a negative diazo-reaction occurred after such drugs as tannic acid, tannigen, and tannalbin had been given.

SIGNIFICANCE OF THE DIAZO-REACTION.—A positive diazo-reaction usually occurs about the fourth day in **typhoid fever**, and it was formerly supposed to be pathognomonic of that disease. Although usually present in typhoid fever, its presence alone does not warrant a positive diagnosis of this disease, while its absence does not indicate a negative diagnosis.

> **Typhoid** bacilli can be found in the blood early in the disease, but less frequently thereafter, contrary to the experiences with the agglutination reaction which increases as the disease progresses. In the 167 cases reviewed, the diazo-reaction was positive in 65.2 per cent.; in 113 cases the leucocytes numbered less than 6000 in 63.6 per cent., up to 10,000 in 32 per cent. and over 10,000 in only 4.4 per cent., including 2 convalescents and an infant. The writer's experience thus emphasizes the diagnostic importance of the diazo-reaction and of hypoleucocytosis. Bacteriologic examination of the blood with Kayser's bile-tubes permitted an early diagnosis in 100 per cent. of the 16 cases examined during the first week. He regards paratyphoid as an entirely different disease from typhoid, his experience confirming the fact that infection is derived from meat, especially pork, or external contamination of foodstuffs, while typhoid is derived from human sources. Minertz (Med. Klinik, Sept. 25, 1910).
>
> When in **typhoid fever** a urine shows the diazo-reaction, it becomes necessary, in order to avoid mistakes, to ascertain whether the reaction is not due to phenolpthalein. As the presence of this drug can be easily demonstrated by addition of alkalies it is only necessary to test the urine with a few drops of some alkali; a pink or reddish color shows the presence of phenolphthalein. If this reaction is negative we have a true diazo-reaction. But in case this reaction is positive (the urine becomes red after the addition of alkalies), we may have the phenolphthalein reaction alone, or a true diazo-reaction, together with the reaction produced by phenolphthalein. In order to test the urine in such a case of a suspected "mixed" reaction, add a few drops of some acid to the test-tube in which there is a positive diazo-reaction. If the color disappears altogether and appears again only after the addition of enough alkali to render the mixture alkaline, the reaction is due to phenolphthalein alone. If after the addition of acid the color becomes lighter, but does not disappear completely and becomes more intense by addition of enough alkali to render the mixture alkaline, the reaction is due to the substance or substances producing the true diazo-reaction and also to the presence of phenolphthalein. Levison (Med. Rec., April 1, 1911).

A positive diazo also occurs in **measles, pneumonia, miliary tuberculosis, scarlet fever, diphtheria, erysipelas,** and rarely in **rheumatism** and **meningitis.**

> Study of the diazo-reaction in **scarlet fever, diphtheria,** and **serum sickness** to determine its diagnostic value in cases of serum sickness exhibiting a scarlatiniform eruption. A large number of diphtheria cases develop serum sickness with rashes of a scarlatiniform, morbilliform, or urticarial nature. The first type offers the greatest diagnostic difficulty, as it develops from the second to the sixth day after administration of antitoxin. Kerr and Rivier found the diazo-reaction invariably absent in scarlatiniform erythema due to serum disease, and the latter found it positive in 56 per cent. of cases of scarlet fever. The writers studied altogether 502 cases as follows: 375 cases of scarlet fever, 56 cases of diphtheria, and 37 cases of serum sickness. The scarlet-fever cases showed the diazo-

Comparative Diagnosis of Typhoid by the Widal, Diazo, and Russo Tests.

	WIDAL.	DIAZO.	RUSSO.
Appears when?	Appears in typhoid fever. Usually after first week.	Appears early in typhoid fever.	Appears in typhoid fever.
Relapses and complications.	Relapses or complications appear to have no effect on reaction.	Reappears with relapses but not with complications.	A positive reaction which grows in intensity probably points to a grave or fatal issue.
Reaction time?	Observations of 2 to 24 hours necessary.	Technic rapidly completed.	Technic rapidly completed.
Acute miliary tuberculosis.	Never present in this disease.	May appear in this disease.	Perhaps never present.
Always present in typhoid?	No.	No.	Yes, perhaps in every case of true typhoid.
In measles?	No.	Sometimes.	No.
In pneumonia?	No.	Sometimes.	?
In malaria?	No.	Sometimes.	No.
In small-pox?	No.	No.	Yes.
Chronic tuberculosis?	No.	Yes. Often occurs late in fatal cases.	Yes.
Effect of drugs taken internally?	None.	It is probable that no drug taken internally gives the true diazo reaction. Certain drugs may interfere with the positive test.	The positive test seems to be given by several drugs, notably urotropin.
Reaction late in typhoid?	The rule.	A diazo test which makes its first appearance after the second week points to acute miliary tuberculosis. When a positive reaction suddenly appears during convalescence a relapse is to be expected.	?
Persistent reaction in typhoid?	Gives no diagnostic nor prognostic information.	May persist throughout infection without any special significance.	Persistent reaction probably spells a bad prognosis.

William (Archives of Diagnosis, Jan., 1912).

reaction positive in 8.53 per cent. The largest number of positive reactions occurred during the first week of the disease, when the rash was present, and gradually diminished and disappeared with convalescence. Uncomplicated cases of diphtheria showed a general average of 5.4 per cent. positive. Rashes in serum sickness gave a general average of 10.8 per cent. positive. Sixteen cases of the scarlatiniform type showed 1 positive diazo, or 6.2 per cent. Of 18 urticarial types 2 were positive, or 11.1 per cent. In 3 cases of the morbilliform type none were positive.

In the 1 positive case of the scarlatiniform type, in which there were no other symptoms of scarlet fever, there ensued an uneventful recovery and no desquamation. The positive diazo here may have been due to the diphtheria. The writers place little value on the diazo-reaction as a point of differential diagnosis, because it is positive in only 15 per cent. of scarlet-fever cases during the first week, and because it was positive in 12.9 per cent. of diphtheria cases during the first week. The reaction was found positive in 75 per cent. of cases of measles. Therefore, a negative reaction in a case of morbilliform eruption would be of value in differential diagnosis between **serum sickness** and **measles**. S. S. Woody and John Kolmer (Archives of Pediatrics, vol. xxix, No. 12, 1912). H.

DICHLORMETHANE. See Methylene Chloride.

DIETHYL BARBITURIC ACID. See Veronal.

DIETHYLENEDIAMINE. See Piperazin.

DIETHYLMALONYLUREA. See Veronal.

DIGALEN. See Digitalis.

DIGITALIS.—Digitalis is officially defined as the dried leaves of *Digitalis purpurea* (Scrophulariaceæ) collected from plants of the second year's growth, at the commencement of flowering. The plant is considered indigenous to central and southern Europe, and is found, among other localities, in the United Kingdom and especially Germany. It grows wild on gravelly or sandy soils in young plantations, at hedge-sides, and in hill-pastures, but is also extensively cultivated. It has been introduced in America, but is still grown rather as an ornament to gardens and in hot-houses than for commercial purposes. Digitalis of excellent quality grows abundantly on the northern Pacific coast of the United States; its collection has, however, as yet not been undertaken, owing to the high cost of labor in that section (Vanderkleed).

The digitalis plant, which is the source of all our medicinal preparations, is a biennial herb with an erect stem twelve to fifty inches in height; numerous drooping, tubular, purple-spotted (occasionally white) or purple flowers, and large, alternate, ovate or ovate-lanceolate, crenate, rugose leaves. The latter are downy, especially on their grayish-green or -brown under surfaces; usually exhibit a purplish midrib, and taper into winged petioles.

The leaves constituting the official digitalis are required to be of the second year's growth, when they are more oval in shape and also more active than those of the first year, and should preferably be gathered either in July or late in June, before the small, round, gray-brown seeds begin to ripen, and when about two-thirds of the flowers have expanded. Notwithstanding these requirements, the time at which the leaves are gathered appears to be of less moment than has hitherto been supposed. According to some experts in these matters, fully developed leaves of the first year plant, collected toward the end of the season, are quite as active as those of the second year. Neither does the locality of growth necessarily exert as great an influence upon the activity of digitalis as has been asserted (Hale), although digitalis growing wild, especially in hilly districts (Butler), is generally believed to be more active than that which is cultivated. Although leaves grown in England have long been considered the best, Hale has demonstrated American leaves to be of equal value.

More important than the factors already referred to are the methods adopted in drying the leaves and storing the galenical preparations. The leaves should be dried in the dark, at a temperature not greatly exceeding 100° C. Properly cured, they exhibit a dark-green hue and an almost total lack of odor, except that generally possessed by dried herbs and leaves, which is frequently described as "tea-like." Once dried, the leaves should be kept in well-filled, dry, opaque and air-tight containers. In the German Pharmacopeia it is specified that both leaves and powder are to be kept over freshly calcined lime, which absorbs any moisture present, and are to be discarded after a period of one year.

However carefully the drug may have been dried and stored, a more or less considerable deterioration, the rate of which cannot be definitely foretold, is likely to take place. This is true likewise of the fluid preparations of digitalis. Furthermore, as obtained by the physician, the fluid galenicals may not only be deficient in strength, but instead may err on the side of excessive potency, largely owing to the evaporation of the menstruum from imperfectly closed containers. Thus Pittenger, testing 51 samples of digitalis tincture, observed a variation in their activity ranging from 30 to 444 per cent. (100 per cent. being standard strength), while 16 samples of digitalis fluidextract assayed at from 26 to 160 per cent. Goodall, testing 23 samples of the tincture freshly made by chemists of repute, found only 12 to be of average strength. In view of these pronounced discrepancies, and the possibility of consequent harm, the physician should invariably demand that the digitalis supplied to him shall have been physiologically standardized, either by the frog-heart permanent systole method or by the minimal lethal dose method in mammals, and that, in the case of fluid preparations, the containers shall have been kept tightly corked. That the standardization shall have been fairly recent is another essential point, since leaves or galenicals assayed a year before may have lost considerable strength during that time. A further danger sometimes arises from the substitution by unscrupulous druggists, in bottles bearing the labels of reliable pharmaceutical houses, of inferior preparations for the original properly standardized contents; such a possibility can, of course, be avoided only by patronizing apothecaries of known reliability.

> Eight samples of digitalis fluidextract, made with 62.5 per cent. alcohol, showed an average annual loss in activity of about 4 per cent. Eleven samples of the fluidextract made with 48 per cent. alcohol showed an average loss of 10 per cent. per year. Six samples of digitalis tincture showed an annual loss of 9 per cent. Houghton and Hamilton (Amer. Jour. of Pharm., Oct., 1909).
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> Among 23 samples of tincture of digitalis examined the limits of the variation were from 275 per cent. over strength to 40 per cent. under. It seems safe to believe that the tincture retains its full activity for one year, but that after that period deterioration is likely to take place. Goodall (Brit. Med. Jour., April 20, 1912).

Hatcher and Eggleston dissent from previous observers as to the deterioration of digitalis preparations.

Report of experimental work indicating that digitalis leaves of good quality do not undergo any deterioration in many instances as the result of age; in a few cases they do appear to have deteriorated, but only with extreme slowness—at a rate probably not exceeding 1½ to 2 per cent. a year. The same holds for the Pharmacopeial preparations made with a menstruum containing at least 50 per cent. of alcohol. Heat below 120° C. does not cause deterioration in digitalis leaves, aqueous infusions, or alcoholic preparations. Liquid digalen is decidedly inferior to the alcohol-containing galenicals in permanency. Digitalis deteriorates in the presence of water. It is irrational to dispense the tincture of digitalis already diluted with water, or with an aqueous vehicle. The physician should order the necessary dilution to be made by the patient each time he takes the prescribed dose, or should employ a vehicle containing a sufficient amount of alcohol. R. A. Hatcher and Cary Eggleston (Amer. Jour. of Pharm., May, 1913).

CONSTITUENTS OF DIGITALIS.—The active constituents of digitalis belong to the group of the glucosids,—relatively unstable substances as a rule, from which sugar is set free by certain enzymes or by heating with a dilute acid or alkali. The chief principles were isolated by Schmiedeberg and Kiliani, and are as follows:—

Digitoxin, a crystalline glucosid with well-defined chemical characteristics, insoluble in water, very slightly soluble in ether, freely soluble in alcohol and in chloroform. This is the most powerful acting constituent of digitalis, and is contained in it to the extent of 0.2 to 0.6 per cent.

Assayed by the Keller-Fromme method, the radical leaves of digitalis yield from 0.527 to 0.531 per cent. of digitoxin, the flowers from 0.563 to 0.585 per cent., and the seeds from 0.215 to 0.225 per cent. Barenstein (Pharm. Zeit., p. 128, 1910).

Digitalin (digitalinum verum), an amorphous glucosid considered chemically definite by Kiliani, and stated by him to be soluble in 1000 parts of water. It dissolves readily in alcohol, but only slightly in chloroform and in ether.

Digitalein, an amorphous, glucosidal body, considered a definite compound by Kiliani, but accepted by Kraft only as a generic term for all the active digitalis glucosids that are soluble in water. Thus, there may exist several digitaleins, all having the property just referred to.

Digitophyllin, a crystalline glucosid isolated by Kiliani from the leaves of digitalis, and not present in the seeds. It is soluble in alcohol, but almost insoluble in water. By some it is considered identical with the substance widely used in France, known as "digitaline cristallisée."

All the above are therapeutically active. The following is of little or no value in this respect:—

Digitonin, a substance belonging to the group of saponins, occurring in two forms, respectively crystalline and amorphous. The amorphous form is soluble, but the crystalline almost insoluble in water. The substance is also fairly soluble in alcohol, but practically insoluble in ether and chloroform. According to Kiliani digitonin is present only in the seeds of digitalis. Kraft, however, refers to a similar body which is contained in the leaves. Digitonin possesses the useful property of keeping the insoluble glucosid digitoxin in solution in aqueous preparations of digitalis, such as the infusion, or when the digitalis leaf is taken by the mouth.

Other substances contained in digitalis include *digitin,* an inert crystalline substance; *gitalin,* a physiologically active glucosid; *digitalosmin,* a stearoptene imparting to digitalis its odor and an acrid taste; *digitoflavone,* a yellow pigment; also a red pigment; an oxidizing ferment occurring in leaves recently dried, and ash to the extent of 10 to 16 per cent.

Most preparations of the separated active principles of digitalis on the market are obtained from the seeds.

PREPARATIONS AND DOSE.—The following preparations of this drug are officially recognized:—

Digitalis, the leaves themselves. Dose ½ to 3 grains (0.03 to 0.2 Gm.); average, 1 grain (0.06 Gm.).

Extractum digitalis, U. S. P. (extract of digitalis), prepared by evaporating the fluidextract until it is reduced to a pilular consistence. Dose, ⅕ grain (0.012 Gm.)

Fluidextractum digitalis, U. S. P. (fluidextract of digitalis), prepared by percolation of the powdered leaves with diluted alcohol. Dose, 1 minim (0.06 c.c.).

Infusum digitalis, U. S. P. (infusion of digitalis), prepared by adding to 15 parts by weight of bruised digitalis 500 parts of boiling water, allowing to macerate for one hour, straining, adding 100 parts by volume of alcohol and 150 parts of cinnamon water, and passing enough cold water through the residue on the strainer to make 1000 parts. Dose, 1 to 4 fluidrams (4 to 16 c.c.).

Tinctura digitalis, U. S. P. (tincture of digitalis), 10 per cent., prepared by percolation and maceration. Dose, 5 to 30 minims (0.3 to 2 c.c.); average, 15 minims (1 c.c.).

The active substances present in the infusion of digitalis appear to be almost exactly the same as in the tincture. It is stated, however, that a greater relative proportion of digitoxin is present in the latter and larger amounts of digitalein and digitonin in the former.

The mode of preparation of the infusion is a matter of considerable importance. There is a tendency on the part of certain druggists to disregard the official rules of preparation and merely dilute a fluidextract, which may have been on the shelves for a considerable time and undergone deterioration. This practice undoubtedly results in harm to many patients, and should be controlled in so far as is possible by the physician, who should specify that the infusion he orders is to be made from fresh digitalis leaves. Not only is this advantageous in that inefficiency of the drug is more likely to be avoided, but because, according to an impression generally prevalent, the true infusion has greater diuretic properties than any alcoholic preparation, which are lost if the substitution referred to is practised.

The following unofficial preparations of or derived from digitalis have come into use:—

Digitalin, German (digitalinum germanicum), a mixture of glucosids obtained from digitalis seeds by extraction with alcohol, precipitation with tannic acid, decomposition of the tannate with acetate of lead or zinc, and purification of the residue. The glucosids present are said to include about 50 or 60 per cent. of digitonin, one-tenth that percentage of true digitalin, as well as digitalein. The substance occurs as a yellowish, amorphous powder, and has the valuable property of being entirely soluble in water as well as in alcohol, though it is insoluble in ether and chloroform. It can be given hypodermically, and is claimed not to produce gastric irritation when taken by mouth, except in large doses. The ordinary dosage varies from 1/12 to ⅓ grain (0.005 to 0.02 Gm.); in emergencies, doses of ½, 1, or even 3 grains (0.03 to 0.2 Gm.) may be given.

> In emergency cases where from ¼ to even 3 grains of German digitalin are occasionally indicated, to avoid abscesses and cellulitis it is necessary to dissolve the remedy in about 25 c.c. of normal salt solution for subcutaneous injection. One-quarter to ½ grain doses (0.016 to 0.03 Gm.) do not irritate if diluted with 10 c.c. (2½ fluidrams). This remedy frequently prevents collapse in diseases like pneumonia and typhoid fever, and is valuable in profound surgical shock. Henry Beates, Jr. (Merck's Archives, Jan., 1913).

Digitoxin (digitoxinum), a single glucosid obtained from digitalis leaves by extraction with 50 per cent. alcohol, precipitation of useless material with lead acetate, evaporation of the supernatant fluid, repeated extraction of the residue with ether, and crystallization. Two forms, hydrated and anhydrous, respectively, are obtained, according as the digitoxin is crystallized from alcohol or from a chloroform-alcohol mixture. The anhydrous form is official in the French Pharmacopeia (Codex) as "digitaline cristallisée" ("digitoxine"; "digitaline Nativelle"), and is extensively used in that country. Digitoxin is insoluble in water, but dissolves in 43 parts of 90 per cent. alcohol and is easily soluble in chloroform. If given subcutaneously, digitoxin sometimes produces marked local irritation. The single dose of digitoxin is usually stated as 1/250 grain (0.00025 Gm.), but amounts as large as 1/64 grain (0.001 Gm.) and even 1/20 grain (0.003 Gm.) (Corin) have been given. The maximum daily dose is 1/64 to 1/20 grain (0.001 to 0.003 Gm.). It is to be borne in mind that the digitoxins obtained from different sources vary somewhat in strength. "Digitaline chloroformique" ("digitaline amorphe"; "digitalinum gallicum"; Homolle's digitalin) is a body probably consisting chiefly of digitoxin, and which is completely soluble in chloroform. It was formerly the official French "digitaline," but is now replaced by "digitaline cristallisée." The dose is generally stated to be the same as that of the latter.

> Use of French crystallized digitalin recommended. There are three ways in which it may be prescribed. First, in massive doses. Fifty drops of the 1 in 1000 solution should be given once or twice in one day in those cases where asystole is threatening, and where there are edema, visceral congestion, deficient urinary elimination, etc. After thirty-six to forty-eight hours abundant diuresis sets in, and the cardiac contractions increase in strength. If the action of these doses be insufficient, after an interval of eight to ten days the same quantities may be again administered. Should the cardiac contractions still remain feeble after the disappearance of the edema, 2 to 4 drops of the same solution may be given daily for one to three weeks after a fortnight's interval. Secondly, in small doses. These are indicated in cases of palpitation, cardiac erethism, and for the dyspnea of mitral stenosis (during compensation). From 5 to 10 drops of the same strength of solution should be given daily for five consecutive days, and then omitted for three or four weeks, when these doses may be recommenced. Thirdly, in very small doses as a cardiac tonic. From 2 to 4 drops of the solution may be

given daily for weeks or months, omitting the doses every two or three weeks for one or two weeks. When a rapid action is required, crystallized digitalin dissolved in oil may be injected under the skin, without any subcutaneous irritation; from 1/8 to 1/2 mg. (1/500 to 1/130 grain) may be so injected. Huchard (Jour. des Prat., Dec. 1, 1906).

Digitalinum verum (Schmiedeberg's digitalin), considered a definite chemical compound, has been used with asserted good results, more especially in the milder forms of cardiac insufficiency, by some clinicians. It is best given in dilute alcohol, in which it readily dissolves, but has also been administered in pills. Kobert states the maximum single dose to be 1/16 grain (0.004 Gm.) and the daily dose 1/8 grain (0.008 Gm.), while Mottes recommends that 1/250 grain (0.00025 Gm.) be given every two or three hours. The average single full dose may be stated as 1/32 grain (0.002 Gm.).

Digitol, a "fat-free tincture," *i.e.*, one from which the fixed and volatile oils which are supposed to contribute to the gastrointestinal irritation sometimes produced by digitalis have been removed. Dose, same as of the official tincture.

Digitalone, a sterile, non-alcoholic preparation of the same strength as the tincture, containing chloretone as a preservative, and suitable for hypodermic use. Dose, same as the preceding.

Digalen (liquor digitoxini solubilis), a solution said to contain 1 part of Cloetta's "amorphous soluble digitoxin" in 1000 parts of glycerin and 1600 parts of distilled water, with 7½ per cent. of alcohol added. The nature of Cloetta's principle, which is said to be about 5 times as soluble as crystallized digitoxin and is prepared by a secret process, is not known. Kiliani believes it to be merely an amorphous substance containing a high percentage of digitalein. By some it is claimed to be the form in which digitoxin is present in the digitalis leaf. Digalen may be used by mouth or intravenously; according to Pagliano, intramuscular injections are well borne. Dose, 8 to 32 minims (0.5 to 2 c.c.); maximum daily dose, 96 minims (6 c.c.). Digalen tablets are also available.

Upon extracting the amorphous digitoxin, so called, from digalen tablets and using it in solution in saline, the drug was found to be equal in activity to crystalline digitoxin; the fatal dose per gram of frog was 0.0085 mg. Cary Eggleston (Amer. Jour. of Pharm., March, 1913).

Digipuratum, a greenish-yellow, bitter-tasting powder, obtained by removing about 85 per cent. of the inert and undesirable constituents from an alcoholic extract of digitalis by the addition of ether, petroleum benzin, or other precipitant, and reducing the resulting fluid to a powder by evaporation with milk-sugar. The preparation is biologically standardized and is said to contain 0.4 per cent. of digitoxin and 4 per cent. of digitalin in the form of tannates. Its active components are soluble in weak alkalies, but not in cold water. It is supplied in tablet or powder form, and the average dose is 1½ grains (0.1 Gm.).

Digipuratum is not entirely free from after-effects. The usual daily dose is 3 tablets, but with individuals over 40 years old, particularly with alcoholics, smokers or gouty patients, it is advisable to begin with half the dose, since the stomach frequently will not tolerate larger amounts. The same care is necessary in pronounced arteriosclerosis or contracting kidney. Despite all care, there may be excessive slowing of the pulse with high tension. In about 25 per cent. of the cases treated with digitalis and an equal number of those who received digipuratum there was anorexia, vomiting, eructations, nausea, and diarrhea. On the average, these symptoms developed after 10½ tablets digipuratum or 0.7 Gm. (11 grains) powdered leaves. Severe symptoms of intoxication were seen in only 1 case after digipuratum and 2 cases after powdered digitalis. Veiel (Münch. med. Woch., Sept. 27, 1910).

Over 180 cases of primary heart disease or secondary cardiac involvement treated with digipuratum. The effect on the urinary output was very prompt in most instances. There was no case of vomiting or diarrhea. Boos and Marx (Archives of Intern. Med., April, 1911).

Digipuratum is insoluble in cold water and dilute acids, but it is soluble in 0.1 per cent. sodium bicarbonate. It has about half the toxicity of ordinary digitalis leaves (Schuttler). It keeps well, is uniform in composition, contains all the glucosides of value in digitalis, and causes less gastric irritation than the powdered leaves. Mueller states that its effect is apparent on patients after 0.4 Gm. (6¼ grains) on the second day, and after 0.3 Gm. (5 grains) on the third day. W. E. Dixon (Quarterly Jour. of Med., No. 18, 1912).

Digipuratum hardly ever gives rise to vomiting in cats, even if comparatively large doses are employed. The most rapid absorption was obtained with digipuratum in solution, then came the powder in suspension and then powdered digitalis leaves. The infusion was absorbed almost as well as the digipuratum solution, but remained in the stomach much longer and most readily gave rise to emesis. R. Gottlieb and S. Ogawa (Münch. med. Woch., Oct. 22, 1912).

Digitalysatum, a fluid prepared by dialysis from the fresh undesiccated digitalis plant. Each gram (16 minims) is stated to represent 0.12 Gm. (2 grains) of powdered digitalis leaves. The product contains 12 per cent. of alcohol. It is employed in doses of 5 to 15 minims (0.3 to 1 c.c.), internally or subcutaneously.

MODES OF ADMINISTRATION.—Oral.—Digitalis is usually administered by mouth, either in the form of the tincture, the infusion, or the powdered leaves. The question as to which of these preparations is the best has given rise to much discussion. Most clinicians consider that where both cardiotonic and diuretic effects are desired the infusion is most efficient, while under all other conditions the tincture should be used. German clinicians, however, manifest a general preference for the powdered leaves, notwithstanding the fact that these are probably somewhat more irritating to the stomach than the other preparations and perhaps less certain in absorption.

> Use of powders containing 1½ grains (0.09 Gm.) of the powdered leaf, 1 Gm. (15 grains) of diuretin, and 0.3 Gm. (5 grains) of sugar recommended. As a rule, one powder is given three times a day for ten days. One or two powders daily, according to the case, may be continued for several weeks. It is best not to give the drug when the patient first comes under treatment, but first to put him to bed, with a milk diet and rest for one to three days. Eichhorst (Deut. med. Woch., Jan. 2, 1905).

The various unofficial preparations of the digitalis glucosids are not, on the whole, considered in any way superior to the official galenicals, except in the fact that glucosids kept in the dry form are likely to preserve their efficiency for a longer time than the leaves, and are thus, where there is no certainty of securing fresh, undeteriorated galenicals, more reliable than the latter. Allbutt, for intermittent administration, speaks favorably of granules of the digitalins of Nativelle or Homolle.

Since the effects of digitalis administered by mouth take several hours to appear and, when once established, last for some days after a single dose, it is unnecessary to give the drug oftener than two or three times daily. It is usually administered with or just after meals, though Worth Hale, having found that the gastric juice tends to impair the activity of digitalis, recommends that the drug be taken between meals and a large quantity of water simultaneously ingested to diminish the resulting gastric irritation. According to Allbutt, combination of the drug with a cordial and light bitter, and requiring the patient to rest for half an hour after the digitalis has been taken, will tend to avoid the production of nausea. The infusion might also be iced, or given in an effervescent preparation. Digipuratum has been stated by several observers to be better borne by the stomach than the official preparations.

The dosage of digitalis is a matter usually requiring very careful consideration. The variations in the amount required in the treatment of different cardiac lesions will be referred to in the section on THERAPEUTICS, but certain general facts may appropriately be referred to here. The chief criterion for judging of suitable dosage is in most instances the degree of relief experienced by the patient from the various symptoms of cardiac inefficiency. While in some cases the dose may have, sooner or later, to be increased to considerably beyond the average amount, the aggregate of the earlier doses, except in emergencies, should be relatively moderate, so that if toxic symptoms appear, destruction of the excess of drug present in the body can be soon effected. The pulse rate should be carefully watched, and the urinary output in particular be observed, any tendency to diminish of the latter—except immediately after the removal of edema with diuresis—leading to a suspicion that the dose given is too large and is inducing renal vasoconstriction. Riegel emphasized the fact that, in chronic myocarditis especially, excessive doses of digitalis might suddenly lead to suppression of urine. Likewise where, in conjunction with pronounced edema, renal activity is poor, toxic phenomena are apt to appear from large doses, and the amounts given should therefore at first be moderate.

In patients who have been taking digitalis for some time, intermission for an undue period is apt to result in a more or less serious setback in the general condition, even though, as is now believed, true habituation to digitalis, other than that implied in an increased ability of the gastrointestinal tract to eliminate the drug unabsorbed, is a practically negligible quantity.

Meyer warns against abandoning digitalis in cases where it does not seem effective at first. Thus, while in acute inflammatory states of the heart the drug is seldom of value, it may yield brilliant results later on. The same may be true in chronic disorders; in particular, where treatment with full doses may have proven a failure, smaller amounts may later be found distinctly beneficial.

> Unless digitalis is pushed no result may be obtained in cases which would at once react to large doses. There is no danger in pushing the drug if the type of case is taken into consideration and the results watched. In most of the author's cases the patient stopped the drug himself owing to the increasing nausea, and the only cases likely to show bad effects are those with damaged auriculoventricular bundle in whom heart block may result. Several cases were treated with doses of 15 minims (0.9 c.c.) three times a day with excellent results. Raised blood-pressure is no contraindication to the use of digitalis, and is often due to some secondary effect of the heart-failure. Turnbull (Brit. Med. Jour., p. 1609, 1910).

Of the drugs not infrequently given in combination with digitalis, nitrites require chief mention. The object in administering such vasodilators is to avoid any blood-pressure-raising effect of digitalis in patients already presenting high tension, especially where there is pronounced arteriosclerosis. Nitroglycerin, given at shorter intervals than the digitalis itself, is most frequently used. Where the blood-pressure, however, is not already high, and vascular changes are not marked, combination of nitrites with digitalis is without advantage and may actually hinder the good effects of the drug. Huchard advised the use of theobromine with digitalis where the pressor effect of the latter is feared, while Traube recommended that in cases of high blood-pressure laxatives be given as a preliminary measure.

> Many writers advise the giving of vasodilators to counteract the constrictor effect of digitalis. It is high time that we discard this hoary tradition. Most of the work done on digitalis has been with toxic doses, and vasoconstriction is one of the toxic effects. It has been shown clinically that in the majority of patients with beginning digitalis effect the blood-pressure falls. Conclusive proof that digitalis in clinical doses relaxes the peripheral vessels has been given by O. Müller and his pupils, who showed with the plethysmograph that there is a constant increase in the volume of blood in an extremity after the use of digitalis. Schmoll (Amer. Jour. Med. Sci., Jan., 1911).

For diuretic purposes such drugs as theobromine and theophyllin, squill, calomel, and the saline diuretics are frequently given with digitalis, the object being to supplement the cardiac and renal vasodilator diuretic effects of digitalis by direct stimulation of the kidney parenchyma or other contributory influences. Whitla considers agurin more effective than diuretin; he points out also that in rheumatic or gouty patients salicylates may be advantageously combined with digitalis for diuretic purposes.

The following pill is advised by Huchard and Fiessinger for combined cardiotonic, cathartic, and diuretic effects:—

℞ *Pulveris digitalis,*
Pulveris scillæ,
Pulveris scammonii....āā gr. xv (1 Gm.).
M. et ft. in pil. no. xx.
Sig.: Four to six pills daily.

> It is often of decided advantage to combine digitalis with ergotin. In this way a pronounced diuretic effect may be obtained even when a combination of digitalis with the modern diuretics has failed. The author uses the following formula:—
>
> ℞ *Pulv. digitalis*.. 1.0 Gm. (15 grains).
> *Hydrargyri chloridi mitis* ... 2.0 Gm. (30 grains).
> *Scillæ* .... 3.0 Gm. (45 grains).
> *Ergotin* .... 4.0 Gm. (60 grains).
> M. et ft. in pil. no. xl.
> Sig.: Four to six pills daily.
>
> If the circulatory disturbance returns and the pills are again indicated, the following formula may be substituted:—

℞ *Pulv. digitalis*	1.0 to 2.5 Gm. (15 to 38 grains).
Hydrargyri chloridi mitis	0.5 Gm. (8 grains).
Ergotin	2.5 Gm. (38 grains).
Scillæ	3.0 Gm. (45 grains).

M. et ft. in pil. no. L.

Sig.: Two pills three times daily. A. Hecht (Therap. d. Gegenwart, March, 1911).

Atropine or belladonna may be used with digitalis where undue vagus stimulation and excessive slowing of the heart are to be avoided, but are disadvantageous in that they reduce secretory activity, thereby impairing digestion, and tend to counteract the diuretic effect of digitalis.

Quinine in small doses is not infrequently of value when combined with digitalis in **chronic myocardial disease,** while iron is indicated in the numerous cases of **valvular disease** in which there is anemia:—

℞ *Tincturæ digitalis,* *Tincturæ ferri chloridi,* of each	fʒiij (12 c.c.).
Acidi phosphorici diluti	fʒij (8 c.c.).
Aquæ chloroformi, q. s. ad	f℥viij (240 c.c.).

M. Sig.: Two teaspoonfuls in a half-glassful of water four times daily. (Whitla.)

Rest in bed and, where edema is present, a reduction of the fluids ingested are valuable adjuncts to digitalis therapy. In severe cases Huchard gave 5 ounces (150 c.c.) of milk mixed with 1⅔ ounces (50 c.c.) of water four times daily for three days, and thereafter undiluted milk, until the patient ceased losing weight from the digitalis diuresis, when solid food was resumed and the amount of fluids increased. Removal of salt from the diet is another procedure which in a certain proportion of cases materially favors the elimination of dropsical accumulations, and may thus assist the diuretic effect of digitalis.

In children digitalis can usually be given in doses slightly larger than would be indicated by Young's rule. Thus, to patients 6 to 10 years old, one-half the adult dose may be administered. For infants 6 months old ¼ to 1 minim (0.015 to 0.06 c.c.) of the tincture may be used (Griffith). As in adults, a close watch should be kept on the action of the drug, and the dosage modified as required by individual peculiarities or the strength of the preparation used. Allbutt refers to the following combination as suitable for children:—

℞ *Infusi digitalis,* *Infusi sennæ,* *Infusi calumbæ*	āā ʒj (4 c.c.).

M. Sig.: Three times daily before meals.

In order to obtain an effect in urgent cases (**pneumonia,** etc.), a baby 1 or 2 years of age should get 5 to 6 *drops* of a good tincture of digitalis every two or three hours until the number of pulse beats has been satisfactorily reduced. In very urgent cases much larger doses may be administered; 15 to 20 drops of tincture of digitalis, repeated once or twice after a few hours, may be safely given to a baby 1 to 2 years old and may prove life-saving. F. G. Oppenheimer (Med. Rev. of Reviews, Jan., 1913).

Hypodermic Administration.—In whatever form used, digitalis is almost certain to cause more or less local irritation when given hypodermically, and this route is therefore, on the whole, useful only for emergency cases, or where with the patient in a serious condition the stomach rebels upon oral administration. Either the tincture or the fluidextract may be used, though both have the disadvantage of including alcohol, itself an irritant. Among the unofficial preparations most frequently employed are digitol (a "fat-free" tincture), digalen tablets, digitalone (least irritating when fresh, as stated by Fussell), and German digitalin. Digitoxin may be injected in the following solution (Unverricht):—

℞ *Digitoxin* .... gr. 1/6 (0.01 Gm.)
Alcoholis absoluti....... ♏c (5 Gm.).
Aquæ destillatæ .... ℥ss (15 Gm.).
M. Sig.: Inject 8 to 16 minims (0.5 to 1 c.c.).

Where there is a "systolic hemic" murmur from profound anemia, digitalis is to be used hypodermically. If it is given otherwise, derangement of the stomach is increased, and this, acting through the sympathetic system, will cause vasoconstriction in the pulmonary system, whence tricuspid insufficiency may result. This condition may arise from a dilated stomach, dilated transverse colon, hepatic congestive conditions, and the arthritic diathesis. If digitalis is to be used in these cases, one should first overcome the congestive disorders by proper elimination. T. H. Stucky (Med. Brief, March, 1906).

In patients badly water-logged, or with high fever and the stomach dilated and inactive, but little digitalis is absorbed and administration by the mouth is useless. Here the drug should be given hypodermically.

The cumulative action, so much talked of especially in former years, is certainly rare. The author has notes of but one case where a sudden poisonous action occurred. M. H. Fussell (Penna. Med. Jour., Nov., 1912).

Strict aseptic precautions are to be taken in administering an injection of digitalis; abscess formation will then seldom occur. The injection should be given deeply. To reduce the local pain, cold compresses are of value.

Rectal Administration.—Where digitalis causes gastric disturbance and hypodermic administration is impracticable, the remedy may be given by rectum, though absorption by this route is somewhat uncertain. Krehl uses for this purpose an infusion of 30 grains (2 Gm.) of digitalis in 5 ounces (150 c.c.) of water, which is mixed with 1⅔ ounces (50 c.c.) of gum-arabic mucilage. The mixture thus obtained is intended for four enemas, two or three of which may be given in a day.

Physicians often persist in administering digitalis by the mouth, when frequent vomiting shows how little hope there is for absorption from the stomach. Two other paths of absorption are readily available: the rectum and the subcutaneous tissues. Half an ounce (15 c.c.) of infusion, per rectum, three times a day, will give about as prompt results as by mouth. Janeway (Amer. Jour. Med. Sci., June, 1908).

Intravenous Administration.—Owing to the insolubility of the more active glucosids of digitalis, strophanthin, which is soluble in water, is better suited for intravenous use, and is generally employed instead. If it is desired to use digitoxin, chloroform or alcohol, or both, will have to be employed to keep it in solution, according to the variety of glucosid to be injected.

INCOMPATIBILITIES.—Digitalis is incompatible in fluid preparations with salts of iron and lead, and with cinchona. It is likewise incompatible with tannic acid and all vegetable solutions containing it.

CONTRAINDICATIONS.—Absolute contraindications for digitalis are few. The most positive are aortic aneurism in its later stages, partial heart block, cerebral hemorrhage, and recent embolism.

In the presence of pronounced arteriosclerosis caution in the dosage is necessary, and where the blood-pressure is very high it is probably best under most circumstances not to administer the drug. The capacity of digitalis directly to raise the blood-pressure by constricting the vessels, however, appears, on the whole, to have been unduly emphasized. Riesman points out the fact, moreover, that in cases of "high-pressure hypertrophy," viz., where the blood-pressure is high and the heart enlarged owing to some obscure cause, but the arteries remain soft, dyspnea and vertigo are frequently relieved by small doses of digitalis, *e.g.*, 5 to 10 minims (0.3 to 0.6 c.c.) of the tincture or ¼ to 1 grain (0.015 to 0.06 Gm.) of the powdered leaves, three times daily.

> Digitalis is absolutely forbidden in cases of partial heart block. We should hesitate to use it in cases of recent emboli, cerebral hemorrhage, aortic aneurism and uremia, unless the need for it is imperative. In the tachycardia of hyperthyroidism and of cardiac neurosis it is useless and may do harm. Occasionally idiosyncrasy is encountered. A. E. Taussig (Interstate Med. Jour., Aug., 1912).

> In aneurism of the arch of the aorta digitalis is contraindicated as a rule, but in certain cases where the heart is failing badly digitalis will tone up the heart and prolong life. Under such circumstances it does not appear to harm the aneurism. M. H. Fussell (Penna. Med. Jour., Nov., 1912).

In cases with cardiac fibrosis (chronic myocarditis) and especially fatty degeneration digitalis is inefficient in proportion to the degree of morbid involvement, but is by no means absolutely contraindicated when signs of insufficient cardiac activity appear. The chief precaution to be exercised where these conditions are suspected is to use relatively small doses, in particular where the myocardial changes are considered to be very pronounced.

The irritant effect of digitalis in the stomach contraindicates its administration by mouth in the presence of gastric inflammation, unless there are urgent reasons for its use.

> Dropsical patients who have taken large doses of digitalis for some time should be tapped with care, for the sudden withdrawal of the fluid may cause absorption of enough of the drug to poison the patient. Digitalis should not be given in instances of acute gastric disturbance, since the drug is irritant to mucous membranes. Here the therapeutic effect of the drug may be obtained by applying a poultice made from the leaves to the loins. Zemp (Jour. Amer. Med. Assoc., vol. xlix, p. 1349, 1907).

Not properly classifiable as contraindications, but none the less requiring emphatic mention, are certain conditions in which, though digitalis may or may not actually be indicated, according to circumstances, the physician is often tempted to administer the drug as a matter of routine, without stopping to inquire whether or not its use is warranted in the individual case. Among these are such vague conditions as "heart disease" in general, murmurs, palpitation and pain in the precordial region, none of which indicate digitalis except under certain definite conditions, to be set forth in the section of this article on THERAPEUTICS.

Caution is also required, in administering digitalis to a patient seen for the first time, to make sure that he has not just previously been taking the drug in large amounts, as it is by no means impossible to witness digitalis intoxication and even death (Eggleston) as the result of summation of the effects of large doses.

This is all the more imperative since some of the forms of cardiac irregularity resulting from digitalis itself can easily be mistaken for those actually due to disease of the heart, and the new attendant will at once naturally think of subduing the disturbance, as, *e.g.*, in auricular fibrillation with full doses of digitalis.

A patient taking digitalis should be carefully watched, especially the pulse. If the latter drops below 60 the drug should be suspended. It should also be discontinued when bigeminal heart action is present; this is most frequently observed with mitral lesions. Where, under digitalis, the amount of urine increases very rapidly, delirium may be observed, even although no digitalis is being taken at the time. This delirium might be ascribed to an autointoxication from absorption, as it coincides with the subsidence of the edema. Eichhorst (Deut. med. Woch., Jan. 2, 1905).

In febrile diseases terminating by crisis, one should avoid the administration of digitalis for twenty-four hours before crisis occurs, and begin again soon after. T. H. Stucky (Medical Brief, March, 1906).

Case of a man who was admitted to a hospital in a condition of marked digitalis intoxication. For eighteen days he had been taking daily 4 powders each containing 0.1 Gm. (1½ grains) of digitalis leaf and 0.5 Gm. (7½ grains) of diuretin. Besides, while still at home, he had been given for three days, in addition to the powders, 2 granules of 0.0001 Gm. ($\frac{1}{650}$ grain) of "crystallized digitalin." The hospital interne, seeing a man markedly dyspneic and dropsical, prescribed further 50 drops of digalen. The breathing was of Cheyne-Stokes type, the pulse-rate 36 to 38, and upon auscultation, in addition to the usual heart sounds, two somewhat weaker sounds were heard at each cycle. That a typical coupled and even triple beat was present was illustrated by sphygmography. The blood-pressure (Pachon instrument) was 210 mm. Hg. The disturbance of rhythm persisted for over ten days, then gradually disappeared, while the pressure fell to 180 mm. Injection of 0.002 Gm. ($\frac{1}{32}$ grain) of atropine during the period of coupled beats brought about no change, illustrating the fact that the action of digitalis is exerted much more on the heart itself than on the nerve-centers. Roch (Revue méd. de la Suisse rom., Feb., 1913).

PHYSIOLOGICAL ACTION.—**Locally,** digitalis acts as an irritant. Thus, when applied to the mucous membranes it may cause redness and pain, and, if given subcutaneously, inflammation, leading occasionally to the formation of an abscess, even though no infective organisms have been introduced at the time of injection. The several glucosids appear to differ in their irritant properties, digitoxin being the most active, while digitalin is relatively but slightly irritating.

The digitalis bodies vary widely in the degree of the direct irritant action they exert on a given mucous membrane. Moreover, one of these agents may be intensely irritant to the mucous membrane of one area in a certain animal and yet without appreciable influence on the mucous membrane of another area. Hatcher and Eggleston (Jour. of Pharm. and Exper. Therap., Nov., 1912).

In the stomach, even moderate doses, especially when continued for some time, tend to induce a more or less marked irritation. The symptoms witnessed are not believed to be wholly due, however, to the local effect, as the drug is known to stimulate directly the vomiting center. This question will be considered further under UNTOWARD EFFECTS (*q.v.*).

General Effects.—*Nervous System.*—The nervous effects of digitalis are limited, probably even with the largest poisonous doses, to the medulla and its contained centers. Moderate doses stimulate only the cardioinhibitory and vasoconstrictor centers. Larger doses, such as are frequently used in animal experimentation, excite, in addition, the vomiting and respiratory centers. Emesis occurs in those animals, such as the dog and cat, which are able to vomit, and in all, at a rather late stage in the poisoning, there is frequently noticed an acceleration in the breathing, the rate of which may be so increased as nearly to equal that of the heart. This respiratory change is probably not wholly due, however, to a direct effect of the drug on the center, but, at least in the more severe or actually fatal cases of poisoning, to the venous character of the blood, which very evidently plays an important part in bringing on the final lethal result; the respiratory acceleration—at first often with maintenance or an actual increase of depth—may thus in some cases be looked upon as an expression of physiological compensation rather than as the direct effect of the drug on the centers. The convulsions sometimes witnessed late in digitalis poisoning are believed due, at least in some instances, to medullary stimulation.

In the frog the reflex excitability of the spinal cord is often diminished by digitalis.

Circulation.—The circulatory effects of digitalis are of paramount importance. In therapeutic doses the drug acts, in the first place, as a powerful stimulant to the myocardium itself. It increases the irritability, tonicity, and contractile power of the heart, although the conductivity, *i.e.*, the ease with which the impulse of contraction passes from one part of the muscle to the next, shows a tendency to diminution, especially with larger doses. This change appears to be related, however, at least in some cases, to the second fundamental effect of digitalis, viz., that of stimulating the vagal cardioinhibitory apparatus, both centrally (in the medulla) and peripherally (in the heart). The third circulatory action of the drug, scarcely less important than the first two, is that on the blood-vessels, which, with certain significant exceptions, are caused to contract, both through stimulation of the vasoconstrictor center and a direct stimulating action on the walls of the smaller vessels.

The functional effects produced by digitalis are due to the simultaneous operation of the three factors just mentioned, which tend respectively, to increase the force of the heart beat, to slow the cardiac rate, and to raise the blood-pressure. With very small doses of digitalis, the effects may be exclusively those of the first factor, the heart muscle being mildly stimulated, but the rate unmodified except in certain susceptible individuals, in whom it may be actually increased. With somewhat larger doses the characteristic "therapeutic action" of digitalis appears,—a product of the combined muscular and vagal effects. In this condition the heart undergoes a greater degree of expansion during diastole, contracts more completely at each systole, and shows a diminished rate. The pulse wave is consequently much larger. Notwithstanding the slowing due to the vagal factor, the amount of blood delivered from the heart into the aorta in a given period of time may be increased. In abnormally dilated hearts, which already contain an excess of blood, digitalis lessens the capacity of the heart owing to the great improvement in tone it produces; but this does not exclude an increase of output, for the process of evacuation during systole is far more perfect than before.

> The members of the digitalis series produce an acceleration of the blood-stream, followed by a retardation which appears under larger doses of the drug. In the greater circulation the peripheral stream is accelerated, while in the portal area there may be a similar effect if these vessels are not strongly contracted. If there is a very great contraction here, as shown by a marked rise in blood-pressure, the portal stream is probably retarded, although a certain amount of resistance may be overcome by the increased efficiency of the heart. The acceleration of the blood-stream during the early stage of the action may explain some of the benefits derived. The fact that the blood is flowing more rapidly through the tissues would indicate an improved blood-supply, giving not only more nourishment, but also providing for more complete removal of waste products. Edmunds (Amer. Jour. of Physiol., Feb., 1907).

That the diminution of cardiac rate caused by digitalis is chiefly due to vagal stimulation is shown by the fact that when the vagi have been completely paralyzed beforehand by means of atropine, which acts on the vagus terminals in the heart, the latter is not slowed by digitalis, but usually accelerated. If, instead of atropine, mere section of the pneumogastrics be practised, however, slowing still occurs (to a variable extent) after the administration of digitalis. This shows that, under ordinary conditions, the cardioinhibitory stimulation is exerted not only in the medulla, but in the heart itself. In the frog, atropinization does not prevent digitalis from slowing the cardiac rate (Böhm); conditions are therefore somewhat different from those existing in the mammal.

> The slowing of the pulse observed after intravenous injection of substances of the digitalis group, due to stimulation of the vagus, is partly dependent upon the rise of blood-pressure produced by these substances in suitable dosage. This rise of blood-pressure may exert a weak stimulating action upon the intracardiac inhibitory apparatus of the heart; but its chief effect is slowing of the pulse by way of reflexes passing from the sensory nerve terminations in the heart through the vagus to the vagus center. An increase of intracranial pressure—as might result in stimulation of the vagus center—does not enter into consideration in the causation of the slowing of the pulse rate. The heart being still considerably slowed, as compared to the normal standard, after exclusion of the rise of blood-pressure, and increase of intracranial pressure not participating in the vagus stimulation, the diminution of the pulse rate may be interpreted in part as a direct effect upon the vagus. The stimulation of the vagus by digitalis is to be interpreted as a central and peripheral effect. No peripheral effect upon the vagus could be observed with strophanthin. Digitoxin has a weak and inconstant influence upon the periphery of this nerve. Adonidin, in the majority of cases, produces a moderate stimulation of the intracardiac vagus terminations. Kochmann (Arch. internat. de pharm. et de thér., vol. xvi, 1906).

> In some people the vagus nerve does not respond to stimulation by digitalis and one sees no reduction in the pulse rate. The counting of the pulse alone will, therefore, give no light as to whether digitalis acts in such cases. Pfaff (Boston Med. and Surg. Jour., May 17, 1906).

> By the use of a "stromuhr" to estimate the volume of blood expelled by the heart per second, and the determination of the blood-pressure and pulse rate before and after the injection of

digitalis or strophanthus, the author is led to state that the increase in arterial tension caused by these agents is due chiefly to a contraction of the peripheral blood-vessels. The part played by the augmented output of the heart per second is considerably less important and generally occurs only during the period immediately following the injection, before the pressure has reached its maximum. C. Tigerstedt (Lancet, May 25, 1907).

The slowing of the normal heart rhythm under digitalis is generally, but not invariably, inhibitory in origin. The slowing in auricular fibrillation does not arise from stimulation of the inhibitory center; in fact the inhibition is less active during the slow pulse than before or after the digitalis action. Experiments do not encourage the belief that the slowing of the pulse in this irregularity is due to failure in the passage of impulses through the auriculoventricular bundle. The heart in these cases is rapid, partly, perhaps, because it is irritable; it is half-starved, and the digitalis, by improving the contraction, may do something by way of improving the nutrition, and thus making the ventricle indirectly less excitable and less receptive for auricular impulses. Cushny (Proceed. Royal Soc. of Med., July, 1912).

Both systole and diastole are lengthened when the heart is slowed by digitalis; the difference is more marked, however, in the latter than in the former portion of the cardiac cycle, the result being that the total period of diastolic rest experienced by the heart in a given time is increased at the expense of that of systolic activity—a condition highly favorable to improved cardiac nutrition.

The blood-pressure often shows little or no change after small or even moderate doses of digitalis in the normal human subject. Favoring a rise in blood-pressure are: (1) The increased output of blood from the heart. (2) Contraction of the vessels. The first of these factors is the resultant of two opposed conditions, viz., the increased amplitude of the individual beats and the lowered rate. If these are exactly equivalent, as appears frequently to be the case, the efficacy of this factor will be annulled. Furthermore, if an increased output of blood does, indeed, occur, other changes may indirectly take place which will counteract any effect this might have on the blood-pressure. As suggested by Cushny, alterations in the amount of blood supplied to the vasoconstrictor center induce variations in its activity in response to the blood requirements of the tissues in general. Where more blood is supplied to the center, as would be the case were digitalis increasing the cardiac output, the center would not be called on as much to maintain tone in the peripheral vessels, and, the walls of these relaxing, a tendency to a general reduction in blood-pressure would be present. Another factor that may be operative in preventing a rise of blood-pressure, and which may, indeed, cause an actual fall, is, in the presence of heart disease with stasis, the removal of the excess of carbon dioxide in the blood which is effected through the improved circulatory condition brought about by digitalis. Carbon dioxide, as in asphyxia, stimulates the vasoconstrictor mechanism and raises the blood-pressure; hence when the excess is removed, the proportion in the blood sinking to normal, the blood-pressure falls. According to A. W. Meyer, of Heidelberg, a reduction in the blood-pressure, previously abnormally high owing to stasis, has frequently been observed after the administration of digitalis.

A rise in pressure due to the drug was, on the other hand, witnessed in but few cases by this author.

> Strophanthus is often said to have less tendency to raise the blood-pressure than digitalis, but in patients neither induces any rise of pressure, and in some individuals, the two cause an equal fall. There is, on the whole, rather less tendency to headaches, nausea and vomiting under strophanthus and squills than under digitalis, but the difference is not very marked and headache is caused in some cases by all three. Slight diarrhea has followed the use of squills more than the others, and strophanthus also tends to cause this more than digitalis. This tendency to diarrhea is still more marked from the use of helleborein and apocynum. A. R. Cushny (Amer. Jour. Med. Sci., April, 1911).

> The authors studied clinically the effect of digitalis on the blood-pressure. The pressure was taken in 47 subjects, some normal and the others suffering from some cardiac disease, before, during, and after the administration of digitalis, which was given as the French official 1 : 1000 solution of crystallized digitalin (really a preparation of digitoxin) in doses of 10 to 30 drops (0.6 to 1.8 c.c.) for several consecutive days. The drug apparently acted in an irregular and variable manner according to the nature of the case. The variations did not depend upon the amount administered and, in fact, occurred even after the drug had been stopped or in those that had not yet taken it. In patients whose pressures had been carefully taken for several days before the ingestion of digitalis, the variations in pressure were neither greater nor less after than before the medication. Thus digitalin, even in repeated full doses, does not affect the blood-pressure, except in cases with myocardial weakness, where the pressure is raised to its previous level owing to the beneficial effect of the drug on the heart muscle. One should not hesitate to use digitalin in cases with arterial hypertension. Josué and Godlewski (Société méd. des hôpitaux; Semaine méd., Nov. 13, 1912).

> Practically digitalis will not raise the blood-pressure in any case. Exceptional instances with an elevation of up to ten millimeters may be met with. One need not be afraid to give the drug in cases of **aneurism** on account of any danger of increasing arterial tension. Norris (Penna. Med. Jour., Nov., 1912).

Of considerable importance from the standpoint of therapeutics are the changes produced by digitalis in the distribution of the blood in the body. Not only is the blood that has accumulated in the venous side of the circulation transferred to the arterial side—owing, at least in part, to the restoration of efficiency in the right ventricle—but there is now known to occur a special constriction of the intestinal and hepatic (including the portal) vessels, which serves both to remove congestion in these organs and to displace the blood into other parts. The intestinal vessels are the first to be constricted. The renal vessels, on the other hand, have been shown by Loewi and Jonescu to be actively dilated by small doses of digitalis.

Before passing on to the toxic effects of digitalis, it is necessary to mention a fourth action of the drug which is of some significance in its therapeutic use, viz., a regularization of the cardiac rhythm when the organ is not beating regularly. This effect is obtained only with therapeutic doses. Larger amounts tend, on the contrary, to bring on arrhythmia where it had not previously been present.

With toxic doses of digitalis, two additional series of effects are superimposed upon those already referred to. The first of these, the so-called second stage of digitalis action, is characterized essentially by a further decrease in the cardiac rate and further vasoconstriction. The heart is so greatly slowed that the output of blood, notwithstanding the fullness of the individual beats, falls below that of the therapeutic stage, and even below that which existed before the drug was taken. The blood-pressure is distinctly increased, at least in the first portion of this stage. Irregularities of rhythm soon after appear, however, and the blood-pressure gradually tends to fall. The arrhythmia appears to be in part due to diminished conductivity in the cardiac tissues, including the bundle of His, which may lead to a lack of synchrony in the beats of the auricles and ventricles. Again, the auricles are believed to contract less strongly than before, and resulting abnormalities in the filling of the ventricles during diastole may account in part for the arrhythmia witnessed. That the vagal mechanism actually is in an extreme state of excitation is shown by the fact that if its terminals be paralyzed by an injection of atropine, the phenomena of the second stage are removed.

In the third stage of the action of digitalis, however, characterized essentially by an acceleration of the heart action, further irregularity and a more or less gradual fall in the blood-pressure, the direct exciting effect of digitalis upon the heart muscle figures more prominently in the phenomena witnessed. The vagal influence is no longer able to exert any effectual control over the ventricular contractions, which run riot and escape all efforts made to maintain proper auriculoventricular coordination. As a result, the efficiency of the heart as a pump is rapidly lessened, and the blood-pressure falls. The condition present in the terminal phase is sometimes termed "delirium cordis." Not only is the rhythm markedly disturbed, but relaxation of the heart in diastole takes place with increasing difficulty, owing to the excessive and progressively augmenting tone of the heart muscle caused by the drug. The final result is complete arrest of ventricular activity; the circulation ceases with the ventricles in the systolic position, but in mammals the ventricular walls immediately relax, so that the usual position of permanent arrest is semidiastole. Not infrequently, in guinea-pigs at least, the auricles continue to beat at a fairly high rate for a number of minutes after ventricular arrest.

In the frog, the typical position of cardiac stoppage is that of systole, the ventricle remaining firmly contracted and pale. It is of interest to note that certain non-vegetable substances, in particular barium salts and bufalin, a glucosid obtained from the skin of certain species of toad, have the same property of causing arrest of the frog's heart in permanent systole.

Respiration.—The direct effects of digitalis on the respiratory center are of no importance from the therapeutic standpoint. Respiration is rendered easier in cases of heart disease indirectly through the improvement in the blood-circulation. With toxic doses, however, the respiratory center appears to share to a certain extent the stimulating effect of digitalis on the vomiting center. At an advanced stage in digitalis poisoning in animals there is sometimes seen a sudden marked increase in the rate and depth of breathing, which, on some occasions at least, appears to correspond to the beginning of poor circulation owing to the toxic action of the drug on the heart muscle. There appear, thus, to be two ways in which the respiratory center may be stimulated: first, directly by the drug, and, second, indirectly owing to the excess of carbon dioxide present as the result of impaired circulation. At the close of poisoning the respiration often becomes slow and shallow; this may be due either to secondary depression of the nervous mechanism of respiration by the drug itself or to the poor supply of blood reaching the centers by reason of the increasing circulatory inefficiency.

Kidneys. — In normal individuals digitalis has only a slight effect on the secretion of urine, but in the presence of heart disease it acts as a powerful diuretic. The drug is not believed to exert a direct stimulating effect upon the renal epithelium and, in fact, no such action is necessary to explain the results produced. In heart cases it acts by improving the circulation. Not only does more blood pass through the kidneys in a given time, the function of these organs being thereby activated, but, owing to diminished venous congestion, the flow of lymph into the blood-circulation,—*e.g.*, from the thoracic duct—is facilitated, effusions being thus drained and the blood rendered hydremic, a condition favoring diuresis.

Until comparatively recent times, the preceding statements would have represented a complete explanation, in so far as was possible, of the diuretic action of digitalis. A feature remaining obscure, however, was the reason why, if the activity of the kidneys is so greatly increased, the functions of various other structures concerned with the elaboration of fluids are not similarly enhanced by digitalis. In 1908 this gap in our knowledge of the drug's action was filled through the investigations of Jonescu and Loewi, who showed that small amounts of digitalis bodies caused an active dilatation of the renal vessels, while the blood-pressure remained the same as before or was very slightly raised. The authors attribute the vasodilator effect in the kidney to direct excitation of the terminals of the renal nerves. When to this action of digitalis are added the improvement in the general circulation, the reabsorption of edematous fluid with resulting hydremia, and the displacement of blood from the intestinal walls and liver by virtue of the vasoconstrictor effect digitalis is known to exert in these parts, it will be seen that several factors cooperate in the diuretic action of digitalis.

> The diuretic effects of digitalis may be produced with no perceptible change in the heart. Mackenzie (Heart, vol. ii, 273, 1911).
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> The diuresis induced by digitalis is the result both of a stimulating action on the heart, manifested in an increase of the pulse pressure—*i.e.*, of the difference between the systolic and diastolic pressures—and of a vasodilator action in the kidneys, most clearly indicated by a diminution in the diastolic pressure. The drug is thus both indirectly and directly diuretic. Digitalis tends to cause an increase of the viscosity of the blood; this, after the resorption of edema, tends automatically to check diuresis, which might otherwise become excessive. Martinet (Presse méd., Oct. 5, 1912).

Another fact to be remembered is that where the amount of digitalis in the system exceeds a certain limit, the renal vasodilatation gives way to constriction. Notwithstanding the persistence of the other factors favoring diuresis, the latter then becomes impossible because the blood-supply to the kidneys is subnormal. The only course remaining under these conditions is to stop the drug and wait until a portion of that in the organism has been destroyed or eliminated, when diuresis will reappear.

> The diuresis produced by digitalis in ordinary doses of the pharmacopeial preparations does not make its appearance before the third or fourth day of administration. When digitalis fails to produce diuresis in **cardiac dropsy** the use of it is not to be abandoned, but it is to be given in larger doses. [Not always.—Ed.] Digitalis which is acting or has acted as a diuretic in cardiac failure must not be suddenly taken away, and must be slowly, not rapidly, reduced in dose before its final removal. Measuring the volume of urine is a ready, accurate, and sufficient index both of the patient's condition and progress. J. Mitchell Bruce (Brit. Med. Jour., Jan. 6, 1906).

> A man aged 52, with an old double mitral affection, pulsation in the jugular and auricles, and a radial pulse of 40 of very low tension, developed, in process of time, **dropsy** of the legs with scanty urine. Rest in bed for a week had failed to remove the dropsy, and at 9 one evening he was given 15 minims (1 c.c.) of tincture of digitalis of known potency. By 5 next morning diuresis had set in and was kept up by small doses of the drug till the dropsy had cleard away. This was an unusual experience in that the drug acted more rapidly than it is generally believed to do. Gordon Sharp (The Antiseptic, July, 1908).

Temperature.—In large doses digitalis tends to lower the temperature where fever is present. The cause of this is not known. The property is of little practical use, for wherever temperature is lowered in the presence of digitalis the vagal inhibitory effect of the drug on the heart, which is interfered with by fever, asserts itself in marked degree, with the result that a dangerous amount of slowing of the heart rate may occur. Since large doses of digitalis are already required to lower the temperature, the futility of using the drug for antipyretic purposes is evident. According to some, the antipyretic effect of digitalis is preceded by a transient rise in temperature.

Metabolism.—Digitalis does not appear to exert any direct effect on tissue metabolism, though general nutrition, and in particular that of the heart muscle, may be improved through its continued effect. Where the drug is given in the presence of edema due to circulatory weakness, a pronounced discharge of chlorides and urea takes place in the urine, but this represents merely a relief from the preceding retention of these substances in the tissues at large.

> From a study of 12 cases the author concludes that there is a marked leucocytosis after the use of digalen. The increase regularly occurred from seven to eight hours after the injection of digalen, and the number reached within twenty-four hours double the original number of leucocytes counted. This occurs both in patients with heart disease and with pneumonia. The leucocytosis recurs every time a dose of digalen is administered. Other authors have found leucocytosis after injecting an infusion of digitalis into animals. G. C. Mirano (Riforma Medica, June 8, 1907).

Absorption and Elimination.—Digitalis is slowly absorbed, and even when absorbed is slow, it is said, in exerting its effects on the heart. The galenical preparations of digitalis, when taken internally, do not begin to take effect, as a rule, for some hours, and the maximum effect of full doses on the heart is not obtained for forty-eight hours or even, according to the curves published by Eggleston, about three days. This does not mean, of course, that a useful therapeutic effect cannot be obtained before this period has elapsed. Some delay appears to occur, however, in the combination of the active substances of the drug with the heart muscle; from this, as well as from the slower rate of absorption into the blood, arises the difference between digitalis and strophanthus in rapidity of effect.

The effect of the digestive secretions on digitalis taken by the mouth has been shown to have a definite bearing on the proportion of the drug absorbed.

Worth Hale has ascertained by experiments *in vitro* that an artificial gastric juice caused deterioration of the various individual glucosids, as well as of the tincture of digitalis, amounting to about 25 to 35 per cent. in three hours. Believing that certain of the untoward effects seen in digitalis medication may be due to the decomposition products of the glucosids, and in view of the fact that the deterioration was shown to be due chiefly to the hydrochloric acid in the gastric juice, he advises that an alkali be prescribed with digitalis.

> Digitoxin, the most important principle in digitalis, is absorbed from the intestines and not the stomach. The absorption is a relatively slow process, usually not completed before five to six hours; this absorption is still further delayed where there is stasis in the portal circulation. Digitoxin is much more rapidly absorbed from digipuratum than from the powdered leaves. R. Gottlieb and S. Ogawa (Münch. med. Woch., Oct. 22, 1912).

> Report of experiments in rabbits showing the possibility of so habituating rabbits to digitalis administered orally that as much as 30 Gm. (1 ounce) could be given daily without causing death. Symptoms such as paresis and diminished heart rate, appearing early in the experiments, would later disappear, notwithstanding an increase in dose. Neither in acute intoxication nor in the habituated animals could digitalis substances be detected anywhere but in the stomach; it was concluded that the activity of the drug was destroyed in this organ and in the duodenum. Even in the unhabituated rabbit this destruction occurs to a marked degree. The heart and voluntary muscles themselves becomes less susceptible to the effects of digitalis in the habituated animals. C. L. von Lhota (Arch. internat. de pharm. et de thér., vol. xxii, Nos. 1 and 2, 1912).

The fate of the digitalis substances in the system is not definitely known. It appears very likely, however, that, at least in part, they become rather firmly fixed in the tissues, especially the heart muscle. Attempts to detect the principles in the urine have met with but little success; it seems probable, therefore, that these substances are for the most part gradually destroyed in the system.

The slowness with which the effects of digitalis disappear is a matter of common observation. That this is due to an actual persistence of the drug in the body and not to continuance of the effect after its destruction or excretion seems to have been definitely established. As Hatcher and Eggleston showed in 1912, there remains in the tissues after the total disappearance of all signs of the action of digitalis, a large portion of the whole amount absorbed before the administration of the drug had been stopped. That this residual portion, moreover, is not actually present in an inert state, but in what may be termed a potentially active condition, is proven by the fact that if doses smaller than those previously used are given at varying intervals of time after the initial discontinuance of the drug, physiological effects similar to those first noted from the larger doses reappear, *i.e.,* there is a summation of the effects of the added small amounts with potential effects of the amounts previously fixed in the tissues. Thus, in one of Eggleston's cases in which coupled beats had been induced by 3.25 Gm. (50 grains) of digitalis leaf taken in a period of seven days, and persisted for nine days after cessation of the drug, 0.675 Gm. (10½ grains) then given caused the coupled beats to reappear in two days, *i.e.,* eleven days after the last dose of the first course of treatment; during this entire period, furthermore, destruction or elimination of the drug had presumably been taking place. The period following the initial discontinuance in which no digitalis effect can be shown present by means of tracings or even, in the majority of cases, by clinical signs, has been termed by Hatcher and Eggleston that of the "latent action" of digitalis. The possibility of summation of the effects of doses given at relatively long intervals is a factor in the so-called "cumulative action" of digitalis.

> Persistence of digitalis action is due, not to the lasting effects of an injury to the heart, but to the actual presence of the drug in the tissues in active form. Experiments with ouabain showed a much higher and more intense action at once, with more rapid elimination, than was the case with digitalis. Cary Eggleston (Jour. Amer. Med. Assoc., Oct. 12, 1912).

It has been shown in animals that the destruction or elimination of digitalis occurs more slowly when the dose given is very toxic than when it is small. Judging from the clinical experiences of Eggleston this would appear to be true also in man. This observer found that after the administration of doses large enough to bring on untoward signs such as partial heart block and coupled beats, these conditions persisted for three to twelve days after the drug had been stopped. The slow elimination of even relatively small amounts of digitalis was illustrated in the experiments of Marvin, who gave a single dose of 20 minims (1.25 c.c.) of tincture of digitalis to each of 20 men and observed a rise in blood-pressure which reached its height in twenty-four hours and did not finally disappear until after fifty hours.

UNTOWARD EFFECTS AND POISONING.—The untoward effects of digitalis most frequently met with are those representing the so-called "cumulative action" of digitalis. This is defined by Eggleston as "the development under small repeated doses of a drug of symptoms which are much more marked than those caused by a single dose." The condition is essentially one of poisoning in mild degree, and in some instances is characterized by the fact that the unfavorable effects develop entirely without warning, at a time when no action beyond the therapeutic is expected. The cause of cumulation is an excess of intake over outgo or destruction, and its prominence in the case of digitalis seems to be wholly accounted for by the slowness with which the system gets rid of the drug as compared to the elimination of other agents of the same group, *e.g.*, strophanthus. A portion of every dose ingested, even though the latter be small, becoming rather firmly fixed in the tissues, including probably those of the heart itself, a time soon comes when the added effects of the amounts successively fixed surpass the therapeutic level, and symptoms of poisoning therefore occur. The only feature remaining, perhaps, unexplained by the above facts is the suddenness with which these effects occasionally appear. It seems not unlikely that this may be the result, at least in certain cases, of the intervention of other factors, such as: (1) Diminished elimination, owing to deficient renal action; lessening in the amount of urine excreted is itself not infrequently an associated sign of cumulative action, the amount of digitalis present in the body having become so large as to induce renal vasoconstriction, an effect hindering diuresis. (2) More rapid absorption of several doses from the alimentary canal owing to some local condition (temporary active hyperemia, or improved circulation, favoring absorption) not previously present. By the co-operation of one or more factors such as these with the slow destruction of digitalis in general, an increased degree of suddenness in the onset of toxic symptoms may obviously be the result. That variations in the rapidity of absorption from the alimentary canal do not account wholly for "cumulative action" is shown by the fact that the latter occurs even upon exclusively intravenous use of the drug.

> The production of the phenomena commonly called "cumulation" of the digitalins depends on the relationships existing among a number of factors, including absorption, elimination and persistence of action, all of which are in need of investigation. The use of the term cumulation tends to perpetuate a misconception. The actions of digitoxin and digitalis persist longer than do those of the other digitalins in common use. The cat shows this persistence of digitalis action much longer than the dog, rabbit or white rat.
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> To avoid accidents, careful regulation of the therapeutic dosage of the digitalins is necessary when they are so used as to elicit action promptly during the period when the action of a previously used digitalin persists, and it must be remembered that every digitalin is a synergist of every other member of the group. There is no sufficient reason for the widespread belief that digitoxin is enormously toxic for man, as compared with other digitalins. The full effects of moderately large doses of digitoxin are not exerted on the heart at once even when they are administered intravenously, but severe symptoms of poisoning may be elicited in a few seconds, and death may occur within two minutes, after the intravenous injection of a very large dose of digitoxin. Hatcher (Archives of Internal Med., Sept. 15, 1912).

The signs and symptoms resulting from an excessive amount of digitalis in the body are referable both to the heart itself and a number of other structures.

Nausea and digestive disturbances are generally among the earliest phenomena to appear. They have usually been ascribed to direct irritation of the stomach by the drug, and, as a matter of fact, the digitalis glucosids do irritate the mucous membranes. Recent researches have indicated rather clearly, however, that the nausea may be due to irritation of the vomiting center in the medulla, and that in the lower animals at least an amount of the drug bearing a certain definite ratio to the lethal dose will regularly bring on centric vomiting. That the fatty substances in digitalis are probably not in any large degree responsible for gastric disturbances is suggested by an experiment of Eggleston and Hatcher, who fed about 2 grains (0.13 Gm.) of the fixed oil of digitalis—an amount corresponding to 70,000 therapeutic doses of the tincture—to a cat without gastric or other symptoms resulting.

Usually the first symptom complained of is nausea, and later vomiting, though at times severe headache is the first and chief complaint. There is frequently a feeling of malaise, with weakness and giddiness on standing, which, added to the anorexia and nausea, give a symptom-complex frequently likened by patients to seasickness. Diarrhea is occasionally produced, but less often by digitalis than by the other members of the group. Rarely digitalis produces mental symptoms, confusion, loss of memory, hallucinations, and at times transient aphasic attacks. Diarrhea, if present, may not subside at once when the drug is stopped and may require the administration of a dose or two of **castor oil,** preferably combined with **opium.** H. Hume Turnbull (Austral. Med. Jour., Oct. 19, 1912).

Where vomiting or nausea occurs after the administration of some digitalis preparation, there may be one of two causes. The principles in the drug may directly irritate the stomach; in such cases the distress is noticed early, even after relatively small doses, and is usually accompanied by salivation (in cats). The digitoxin is generally still in the stomach and has not been absorbed. Or, the vomiting may be a true toxic effect of the drug seen after an excess has been given. Here general symptoms from absorption usually appear after six to seven hours. At this time no digitoxin is found in the stomach. R. Gottlieb and S. Ogawa (Münch. med. Woch., Oct. 22, 1912).

The emetic action of digitalis and its derivatives is usually attributed to direct irritation of the stomach. This is not supported by experimental evidence. The vomiting is due almost entirely to the direct action on the vomiting center in the medulla. In the authors' experimental investigation the smallest amount of any digitalis body that was followed by emesis was about 20 per cent. of the fatal dose, in the case of true digitalin. Of 61 animals receiving more than 30 per cent. of the fatal dose, 41 vomited, and it was remarkable that of the non-proprietary bodies the drug showing the greatest emetic actvity was that which is generally supposed to be the least irritating to the stomach, viz., true digitalin. Digitalis was found to produce emesis in nearly every case when an appropriate dose was administered. The action on the vomiting center cannot be removed from any of the digitalis bodies by any process of purification. Only traces of digitonin are found in the galenical preparations, and they exert no appreciable effect on the stomach after giving therapeutic doses. The employment of opium to prevent the gastrointestinal symptoms of the digitalis bodies, in ordinary cases, masks the appearance of toxic symptoms which should serve as a signal for reduction of the dose. The results lent no support to the claims that digalen, digipuratum, digitalysatum or the fat-free tincture of digitalis are less actively nauseant or emetic in proportion to cardiac activity than galenical preparations of digitalis and strophanthus. C. Eggleston and R. A. Hatcher (Jour. Amer. Med. Assoc., Feb. 15, 1913).

A decrease in the amount of urine passed, or actual suppression, is another frequent and more definite sign of digitalis intoxication. It shows that enough of the drug is present to substitute for the renal vasodilatation caused by small doses a pronounced vasoconstriction, which tends to arrest the renal function. When oliguria appears, digitalis should be discontinued, or, at least, the amount greatly reduced, for this condition may lead to further impairment of digitalis elimination and thus accentuate the toxic effects. Occasionally signs of renal irritation, such as albuminuria, occur in conjunction with oliguria under digitalis.

Headache, with a sensation of "tightness" in the head, and numbness ("emptiness") or coldness in one or more extremities also occur as evidences of digitalis poisoning. They are probably due chiefly to changes in the caliber of the vessels, particularly vasoconstriction.

Dizziness, nightmares, mental confusion, and anemia are likewise not infrequently caused by digitalis. Robertson has seen several maniacal outbreaks follow the use of this drug.

> Some nocturnal delirium is one of the bad results of digitalis. Pallor, coldness of the extremities, trembling, and contraction of the pupils, are important indications to suspend the drug. Some patients die suddenly of syncope, others gradually. Death from digitalis is most frequently met with in Bright's disease, arthritic and anemic subjects, and in persons with aortic incompetence or delirium tremens.
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> Occasionally there is melancholia and night-terrors. An unusual result is pulmonary apoplexy. Potain (Jour. de méd., April 10, 1900).
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> In an experiment on 20 female Belgian hares, which tended to show that large doses of digitalis, continuously administered, will cause slight enlargement of the normal heart, the development of a vicious and carnivorous tendency among the animals which took the digitalis was an interesting feature of the experiment. The animals were at first very docile. As the dosage of the remedy increased they began fighting and biting each other in a most ferocious manner. The two experimental animals which died were found in the morning mutilated and in part devoured. The control animals remained docile. F. B. Wynn (Jour. Amer. Med. Assoc., July 16, 1904).
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> A number of cases have been noted where what was called delirium tremens was found after a time to result from digitalis. The removal of this drug was followed by subsidence of the acute symptoms. In persons of peculiar unstable mental and emotional states digitalis is sure to produce, if taken any length of time, delirium accompanied by hallucinations. These do not seem to be peculiar in any way except in that they resemble those which follow alcohol. Hall (Quarterly Jour. of Inebriety, Oct., 1905).

As regards the heart itself, the most evident signs of excessive digitalis action are pronounced slowing of the cardiac rate—below 55 or 60 beats per minute—palpitation, and a subjective feeling of oppression in the heart region. The slowing is frequently the result of excessive inhibition through the vagi. Various forms of irregularity have also been detected after digitalis. Eggleston classes these, in the order of increasing intensity, *i.e.,* from the effects of larger and larger amounts of digitalis, as follows: (1) Sinus arrhythmia, consisting of periodic waves of slowing involving the entire heart, with subsequent more or less rapid return to the normal rate. This phenomenon is considered due to vagus stimulation. (2) Muscular irritability, associated with the production of extrasystoles or abortive contractions, and due to the direct action of the drug on the myocardium. This disturbance is not as frequently seen as the result of digitalis action as the preceding disturbance. (3) Auricular fibrillation, *i.e.,* loss of co-ordinate contraction in the auricle and its replacement by the formation of independent contractile impulses at numerous points, was brought on by digitalis in a previously regular heart in a case reported by Mackenzie. (4)

Combined phenomena,—*e.g.*, extrasystoles, heart block, and sinus arrhythmia. (5) Heart block, partial or even complete, an expression of the effect of digitalis in lowering the conductivity of the auriculoventricular bundle of His, and manifested by a prolongation of the interval between the auricular and ventricular systoles, in more severe grades by the complete omission of some of the ventricular beats, and in the "complete" form by continuous dissociation between the auricular and ventricular rates, the two portions of the heart beating independently. According to Lewis, the severer grades of partial heart block are not infrequently observed when digitalis or its allies are given in toxic doses to young patients with rheumatic hearts. (6) Coupled beats, the most serious of the untoward actions of digitalis on the heart rhythm. The successive pairs of beats can sometimes be felt at the wrist. This condition is said to occur only in hearts the seat of auricular fibrillation. The minimal amount of digitalis that can produce coupled beats in cases of auricular fibrillation is, according to Eggleston's experience, 2.25 Gm. (34 grains) of the leaves.

> Of the various cardiac irregularities produced experimentally by digitalis, the earliest to appear in most instances is an occasional omission of ventricular contractions, owing to an interruption of the stimulus between the auricles and ventricles. Somewhat later, or even immediately after this, the heart may assume a peculiar rhythm in which the auricles and ventricles are beating quite independently of each other. This irregularity differs from the ordinary rhythm of complete heart block in that the ventricular rate is not slow, but approaches and usually exceeds the auricular rate; so that, for example, one may count 16 ventricular to 15 auricular contractions. This rhythm is common in carefully graded digitalis poisoning in dogs, but had never been described in man until the author's report of a case. The venous tracings taken one day before this patient died showed a regularly recurring cycle of changes. Each cycle required about seven seconds for its completion, and included about 14 ventricular contractions. At certain portions of the cycle, a single, sharp, positive wave occurred in the jugular pulse just after the onset of ventricular systole. Midway between these groups of sharp waves, each ventricular systole was represented on the venous pulse by two waves of almost equal height connected by a more or less distinct plateau. These cycles, from their duration, were evidently independent of the respiration, for the respiratory rate was constantly about 30 a minute. It was found that the patient had been taking drugs of the digitalis series in considerable quantities for a long period. During all this time his heart-failure was gradually becoming worse, although the daily amount of drugs taken did not seem excessive. At no time was marked slowing of the pulse observed. A. W. Hewlett (Archives of Internal Medicine, Feb., 1910).

Toxic effects of digitalis and related bodies may usually be discovered in their earliest stages by careful and frequent sphygmographic observations, and may be divided into three periods with regard to their occurrence and severity: (1) Period of vagus stimulation; (2) period of depression of conductivity with masked vagus action; (3) period of marked muscular irritability with depression of contractility. Muscular irritability may be the first symptom observed, the other stages being short in duration and easily overlooked. This irritability from digitalis must be differentiated from the progress of the cardiac disease by careful observations of combined jugular and radial tracings. With therapeutic doses the rise of blood-pressure due to vasoconstriction is so slight that it may be disregarded, but with toxic doses it becomes of extreme importance. H. C. Bailey (Amer. Jour. Med. Sci., Aug., 1911).

Three cases developed a sinus arrhythmia of high grade under the influence of digitalin. Two of these had a pre-existing impairment of conductivity. One case showed an extreme sensitiveness to the drug, which may have been related to the fact that the auricles had just previously been in a state of fibrillation. Laslett (Quarterly Jour. of Med., April, 1912).

In a proportion of patients with normal rhythm, the drug affects the auriculoventricular bundle more particularly, and this produces partial heart block. Mackenzie (Therap. Record; Med. Standard, July, 1912).

Nausea, vomiting and headache may not be the first indications of full digitalis dosage. Heart block, showing itself only by an occasional dropped beat, may constitute a warning. Slowing of the rate may also be the result of a sinus arrhythmia, which is a vagal reaction. Digitalis may also produce pulse intermission due to extrasystoles. Coupled beats constitute a curious irregularity brought about by this drug. The second beat has been shown to be of the nature of an extrasystole arising in the ventricle, and it may not reach the wrist, so that the pulse rate appears halved. This rhythm may be maintained for days, but is only reached with full doses, and is almost peculiar to mitral disease with auricular fibrillation. Pulsus alternans may also appear with excessive doses of digitalis, and may be regarded as an evidence of excessive stimulation and exhaustion of the heart muscle. Lastly, fibrillation may be caused in some cases of regular rhythm with degenerated muscle; this is also an overaction due to stimulation. Larger, highly toxic doses cause the ventricle itself to fibrillate; there is no co-ordinated ventricular contraction, no output of blood, and death results. It is possible, though not proven, that if sudden death occurs from excessive doses of digitalis, it is due to this mechanism. MacKenzie asserts, however, that if the drug is stopped as soon as vomiting or nausea appears, or the rate falls below 50, no untoward results will arise from digitalis. M. D. Silberberg (Austral. Med. Jour., Oct. 26, 1912).

Hewlett points out the fact that in young persons, in neurotic individuals, and after infectious diseases, the controlling influence of the vagi on the heart is particularly marked and labile. Irregularities associated with excessive vagal action are therefore especially likely to result from the use of digitalis in these cases (Cushny).

Acute poisoning by single massive doses of digitalis is infrequent. The earliest symptoms are nausea and vomiting, the latter violent and repeated, together with headache, dizziness, and visual disturbances. The pulse for a time is rendered slow and powerful, but later tends to become feeble and irregular, and is accelerated when the victim leaves the recumbent posture. Vasomotor changes and altered distribution of blood in the body are betokened by pallor of the face, prominence of the eyeballs, and a blue color of the sclera. Diarrhea is likely to be observed; there may be salivation of central origin; the flow of urine may cease owing to renal vasoconstriction; there may be pain in the extremities or back, and in the later stages of the poisoning dyspnea is a prominent symptom. The body temperature is lowered; delirium may supervene, followed by stupor, and pronounced motor weakness or actual paralysis finally occurs, owing to a curare-like action on the motor nerve-endings. If paralysis is not complete, convulsions may develop. Death, if it takes place, occurs usually in one or two days. According to Wood, the limits in the duration of the poisoning are, respectively, three-quarters of an hour and ten days. Most cases of digitalis poisoning recover.

> A boy 2 years old, one morning obtained a box containing granules of Nativelle's digitalin and swallowed five of them. Each one contained 1/250 grain (0.00026 Gm.). He remained well until evening, when he became unusually cross; early the next morning he vomited repeatedly and became very drowsy. When seen he was semiconscious and pale; pupils somewhat dilated; vomiting small quantities of bile-stained mucus; sweating profusely; extremities were cold, pulse was so irregular and intermittent that it could not be counted, and the respirations were extremely shallow and slow. The patient was given 2 grains (0.13 Gm.) of **calomel** and liberal quantities of **brandy** and water. When seen again, about three hours later, the condition in general was much worse; the child was absolutely comatose. On the evening of the same day there was some improvement, and from that time on recovery was uninterrupted, though slow. Frank Radcliffe (Brit. Med. Jour., p. 338, 1901).

Treatment.—In cumulative poisoning, withdrawal of the drug for some days is generally all that is required. In view of the fact that rising from recumbency to the upright position or exertion of any other kind by patients fully under the influence of digitalis places considerable added strain upon the heart, these cases should be kept as quiet as possible until the signs of excessive digitalis action have subsided.

In poisoning from single toxic doses of digitalis **tannic acid** or **Lugol's solution** may be administered as antidotes. The most important measure, however, is to secure evacuation of unabsorbed poison by **washing out the stomach** or, if necessary, giving **emetics.** The drug is, of course, likely itself to produce emesis. **Magnesium sulphate** should be given to prevent further absorption from the intestinal tract. **Moist, hot applications to the lumbar regions** have been recommended, to favor relaxation of the constricted renal vessels and promote elimination of the drug through this channel. To overcome the general vasoconstriction, with the consequent undue resistance to heart action and tendency to a rise in blood-pressure, **nitroglycerin** in full doses, or **alcoholic preparations,** may be used. In the later stages of poisoning, depression of the medullary centers is an important source of danger; stimulants such as **caffeine** or **hot coffee, strychnine** and **atropine** should therefore be used. **Artificial respiration** should be instituted as soon as dyspnea appears, as it has been shown experimentally that life can sometimes be prolonged for hours in this way or even, occasionally, animals saved from a dose otherwise certainly fatal.

THERAPEUTICS. — Diseases of the Heart.—Digitalis is, on the whole, by far the most useful drug available for the treatment of cardiac disease. It is the typical representative of a group of drugs characterized not so much by their power to stimulate cardiac activity in acute conditions, although this, in itself, forms part of their field of usefulness, as by that of improving the nutrition of the myocardium where it is impoverished or where increased contractile activity is demanded to overcome mechanical obstacles, local or remote. These agents, with their slow-going and more or less persistent influence on the heart, are often termed "heart tonics" in contradistinction to "stimulants" such as ether, atropine, and alcohol, which temporarily reinforce cardiac action chiefly in various indirect ways and do not necessarily leave the heart, after their immediate effect disappears, in a better nutritive condition than they found it.

The improvement in cardiac nutrition brought about by digitalis may be ascribed to several simultaneously operative factors. Thus it is stated that the drug, through the prolonged exciting effect it exerts directly on the heart muscle, improves the coronary circulation by making the beats stronger, and thereby enhances its own blood-supply. Again, slowing of the heart rate through vagus stimulation tends to rest the heart by prolongation of the period of diastole, during which the organ recuperates from the preceding systole. It is a well-known fact that in the presence of rapid cardiac rates the diastolic period in each cardiac cycle is shorter in comparison with the period occupied by systole than is the case when the rate is slow; hence the total amount of rest obtained by the heart under digitalis is increased. According to Hering and Gaskell vagus stimulation also exerts a favorable trophic influence on the heart muscle, directly increasing the anabolic or building up processes in the cardiac tissues. Finally, a by no means inconsiderable factor in the improved nutritive state brought about by digitalis is the interruption of a vicious circle in which the heart's own weakness reacts on the quality of the blood supplied to it. The feebler the heart, the greater the impairment in the pulmonary, gastrointestinal, hepatic, and renal functions, through which the blood is maintained in its normal state of aërative and nutritive efficiency, and low toxicity; the more inadequate the blood itself, in turn, the greater the impairment in cardiac activity. By relieving venous congestion through increased cardiac power, and by bettering the distribution of blood through vasoconstriction in the splanchnic area, the renal vessels meanwhile remaining unconstricted, digitalis breaks into the vicious circle and, where conditions are not too serious, places the heart on the highroad to functional recovery.

> Digitalis acts as a specific on the tonicity of the heart muscle, and is indicated whenever symptoms point to a failure of that function. Its tonic effects are best secured with a dose equal to the amount excreted—about 0.1 Gm. (1½ grains) a day—though doses of 0.15 and 0.2 Gm. (2¼ to 3 grains) a day sometimes can be taken for weeks without the appearance of cumulative effects. Loss of tonicity is shown first by general symptoms—râles over the bases of the lungs, enlargement of the liver, and slight edema of the ankles. Digitalis is indicated, therefore, whenever these symptoms appear, and especially in cases in which the patient, after recovering from a severe break in compensation, shows a tendency to fail on the slightest exertion. A fall in the systolic pressure can often be noted coincidently with an improvement in the general condition of the patient. In anemic cases, when the general nutrition was badly affected, the author found the combination of digitalis with arsenous acid very efficacious; it may succeed when digitalis alone would fail. Emile Schmoll (Amer. Jour. Med. Sci., Jan., 1911).

The above features by no means exhaust, however, the possibilities for good to be thought of in connection with this drug. Since the remaining factors differ according to the particular cardiac affection for which the drug is used, and, still more, because the indications for digitalis vary enormously in the different states, the latter will now be considered *seriatim.*

Cardiac dilatation is perhaps the most direct indication of all for digitalis, since one of the prominent actions of the latter is to increase the tonicity of the heart muscle and hence overcome abnormal distention of this organ. In **simple acute dilatation,** such as results from excessive physical effort, the patient should at first be placed on small doses, the amount then being gradually increased until pronounced benefit is noted; absolute rest should, of course, be simultaneously imposed. In the acute cardiac dilatation of **infectious diseases,** digitalis is less striking in its effects, but is nevertheless frequently of value. Underlying the failure of cardiac power there is, of course, usually an **acute myocarditis,** with perhaps even fatty degeneration of the heart tissue. The more pronounced these myocardial changes, the less useful the drug is likely to prove and the greater the caution required in its employment, except in the final stage as an ultimate resort. As in simple dilatation from exertion, small doses, such as 1 or 2 drams (4 to 8 c.c.) of the infusion should be used at first, unless the phenomena of cardiovascular failure are very acute, when larger amounts may be given together with other stimulants. It is important, in giving digitalis in the course of infections, not to judge of the effects of the drug by a change in the pulse rate, *i.e.,* not to expect slowing, as vagal activity is diminished in fever; the quality of the heart sounds should rather be taken as criterion in regulating the dose. Calcium, in the form of the lactate or lime water, is to be thought of as a useful heart remedy, and, in cases where free use of digitalis is deemed unsafe, should be tried without hesitation. Digitalis is not well suited for cases with pronounced nervous excitement. In **pneumonia** the value of digitalis as a heart tonic has been particularly emphasized, and even its administration throughout the disease advocated.

It is often stated that in **chronic myocarditis** or **cardiac fibrosis,** as well as in **fatty degeneration,** with signs of functional insufficiency of the organ, digitalis is of little or no value. The heart muscle, having been weakened through partial replacement by noncontractile tissue, is said not to be able to respond to the stimulating effect of digitalis and in some instances to be injured rather than benefited by the drug. The alleged effect of digitalis in raising the blood-pressure has also been advanced as a reason for withholding digitalis in these cases, on the ground that undue resistance to the heart action is imposed. It has of late become evident, however, that digitalis, except in a few instances, has little or no effect on the blood-pressure, which may, in fact, be somewhat reduced. Many clinicians, moreover, advise its use. Thus Abrahams states: "Patients with myocarditis can stand 15-drop doses of the tincture three times a day very nicely. It does them a great deal of good." In view of these facts, it would appear that the dangers attending the use of digitalis in chronic myocarditis have been overdrawn, and that with due caution as to dosage, more particularly where there is reason to suspect pronounced fatty changes, there should be little hesitation in employing the drug. By some strophanthus is given preference over digitalis in these cases, with the idea that the vessels are less constricted by the former than the latter. There is reason to believe, however, that too much stress has been laid on this difference between the drugs. Where it seems especially desirable to avoid any increase of blood-pressure, nitrites may be given with the digitalis (preferably at shorter intervals, since their effect is of brief duration).

> The good effects of digitalis on the tone of the heart muscle are most often seen in cases with a history of rheumatism, which disease seems to leave usually a fair amount of sound muscle, allowing of recovery even from considerable distress, while in hearts in which the muscle is degenerate from old age, insufficient blood-supply, or chronic toxemia, the response is very much less or even totally absent. In this latter group of cases slowing is very rarely seen, and the vagal action seems to be absent, though in rheumatic cases rarely slowing may be marked. H. Hume Turnbull (Austral. Med. Jour., Oct. 19, 1912).
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> In cases with the senile degenerative type of heart, the activity of the inhibitory center is very low. An injection of atropine will raise the rate only about 4 beats per minute, and one cannot get much vagal effect from digitalis. Again, if the heart muscle is of poor quality, one cannot expect it to respond to digitalis by improved nutrition. These cases, therefore, are not in a favorable position to respond to digitalis, and only a few do respond. In those that do, one may assume that the heart muscle is relatively good. In the child, vagal inhibition is also slightly developed, and atropine has little effect in raising the heart rate. But here the heart muscle is good, and when digitalis is needed the response is good. M. D. Silberberg (Austral. Med. Jour., Oct. 26, 1912).
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> In **myocardial degeneration** from any cause, it is the author's practice carefully to note both the apical rate and the pulse rate at the time the patient is put to bed. If no slowing of the rate occurs, and no lessening of the tendency to abortive systoles takes place, as evidenced by the discrepancy between apical and pulse rate, in the majority of the cases one will find that digitalis cannot be used at all, or, if used, is disappointing in its effects. W. E. Robertson (Penna. Med. Jour., Nov., 1912).

Chronic myocarditis generally occurs in association with other more or less evident organic lesions, and in particular with arteriosclerosis. Where this condition is marked, digitalis should, of course, be used only with some circumspection. If the blood-pressure is not much raised, however, and there coexist pronounced symptoms of circulatory inefficiency, digitalis in small doses, it is now conceded by many, will often yield excellent results. In cases with marked emphysema and cyanosis, however, special care is required, as large doses of digitalis may cause sudden death. In these cases German clinicians prefer to use caffeine and theophylline sodium acetate (theocine).

> In cases with high arterial tension digitalis is at first contraindicated; but in all these cases in course of time symptoms of heart-failure set in. In both cases at this period benefit may be obtained from the careful use of digitalis or strophanthus. It is often advisable to administer at the same time one of the vasodilators or the iodides. Formerly, the author employed the vasodilators alone or gave digitalis only in small doses, combined with full doses of the nitrites. He found, however, that in many cases he had no results unless he increased the amount of digitalis until full doses were reached and the blood-pressure had gained its former level; only then did edema disappear. In such patients digitalis is often demanded in fairly full doses to maintain blood-pressure at its high

level, otherwise capillary circulation fails and venous stasis develops. A. D. Blackader (Therap. Gaz., Oct., 1908).

In cases of **arteriosclerosis** with vasomotor control largely gone, the blood-pressure may be found, for instance, to be 280 mm. Hg in a case in which, the heart beginning to fail, there is some edema of the ankles and shortness of breath upon ordinary exertion. It might be thought that the best treatment would be to give drugs to diminish the blood-pressure. In practice, however, the best results are obtained by giving 15 minims (0.9 c.c.) of tincture of digitalis in water three or even four times a day. The blood-pressure will very likely rise from 280 to 300 mm. Hg, but at the same time the patient's sense of well-being will increase. His edema will disappear, his breathlessness will vanish, and he will be better fitted for his ordinary avocations than upon treatment designed to diminish his blood-pressure.

It might be thought that he would necessarily suffer from apoplexy, but in practice it is found that the risk of this does not seem to be any greater with the giving of the digitalis than without it. French (Clinical Jour., July 5, 1911).

Using doses of tincture of digitalis certainly large enough to be active, viz., from 15 to 20 minims (0.9 to 1.25 c.c.) three or four times a day, and continuing until distinct evidences of general action were present, the author found that there was only in one instance a rise of blood-pressure, and in several there was a fall. The patients numbered 21, and were suffering from various forms of valvular disease with more or less ruptured compensation. Not infrequently a normal diurnal variation in pressure, of considerable range, occurred. The internal administration of digitalis apparently does not raise the blood-pressure in man by constricting the peripheral vessels. If this be so, there is no risk in administering the drug in cases of degeneration of the walls of the blood-vessels or of supernormal blood-pressure. Price (Brit. Med. Jour., Sept. 21, 1912).

In the frequently met subjects of combined circulatory and renal involvement or "**cardiovascular-renal disease**," at a stage where, with the blood-pressure still high and the kidneys secreting urine of low specific gravity, the heart begins to fail and edema to appear, moderately large doses of digitalis will often bring considerable relief, the heart muscle itself being generally better preserved than in other myocarditides. According to A. Meyer it is especially the cases with distinctly high blood-pressure that require fairly generous amounts of digitalis. Where the renal excretory function is already seriously compromised, however, full doses may bring on uremia by arresting the flow of urine. Hence it will not infrequently become a question whether digitalis should be used at all in these cases, small doses alone generally proving inefficient in overcoming the cardiac weakness.

Meyer suggests that where the vascular changes accompanying myocarditis are but slightly marked, 0.1 Gm. (1½ grains) of powdered digitalis be given thrice daily for a few days, then once or twice daily. Where they are more pronounced, or the patient's age is such as would lead one to suspect their presence, greater caution should be exercised, 0.2 to 0.3 Gm. (3 to 4½ grains) being given *per diem* for two or three days only, then 0.1 Gm. (1½ grains) for a day or two. Combination with a diuretic, at the beginning of treatment, may be advantageous.

Valvular Disease.—Consideration of the uses of digitalis in valvular disease may properly begin with **acute endocarditis**, since this is the natural precursor of deformity of the valves. The consensus of opinion is that digitalis should not be used in this condition until indications of actual heart weakening occur. Where the heart muscle is less impaired than the valves, as is usually the case, it seems clear that increasing the force of the heart beats with digitalis may be productive of more harm than good. The same applies to cases of **subacute endocarditis,** in which the inflammatory process in the endocardium and valves continues for weeks or months, with some febrile reaction and chills at irregular intervals. Rest in bed is the most important measure in the treatment of these cases.

> In acute endocarditis especially, but also in acute myocarditis, the employment of digitalis is to be deprecated. In this condition absolute rest with low vascular tension is demanded; even regurgitation of the blood-stream is of value for the time being by lowering intraventricular pressure. All acute inflammatory symptoms must pass away completely before the administration of digitalis can be free from risk of harm. If stimulants to the general circulation at this time are demanded, strychnine, ammonia, camphor, and alcohol are to be preferred. A. D. Blackader (Therap. Gaz., Oct., 1908).

> As a rule in the **heart-failure of acute rheumatism** with failure of tonicity, while the infection is acute digitalis fails entirely, but at a later stage, when the temperature has been normal for some days, and dilatation increases with dropsy, its administration is sometimes of great value. H. Hume Turnbull (Austral. Med. Jour., Oct. 19, 1912).

In **chronic endocarditis,** with gradually developing valvular fibrosis, or in cases in which defective valves remain as they were after subsidence of an acute or subacute inflammatory process, myocardial hypertrophy usually occurs to compensate for the mechanical disadvantage at which the heart is placed owing to the valvular trouble. Where this compensation is sufficient to satisfy ordinary circulatory requirements, digitalis is rarely indicated. As soon as signs of cardiac insufficiency, such as dyspnea or cough on exertion, palpitation, slight edema, and indigestion appear, however, and most emphatically where the patient has already taken to bed when first seen, digitalis should be administered, and will often be productive of a remarkable degree of benefit. The indications for the drug vary somewhat in the case of lesions of the different valves, and the latter will therefore be taken up individually.

It is in **mitral insufficiency,** the commonest form of valvular involvement, that digitalis is most strikingly effectual and may be given with the least danger. As in every other cardiac disorder, the drug is especially valuable where dilatation of the cardiac walls can be detected by physical methods of examination, the tonifying property of digitalis rapidly drawing the insufficient ventricular walls together and increasing the functional efficiency of the organ. The prolonged diastole rests the muscle, the powerful systole improves the coronary circulation, and the increased tone may result in contraction of the mitral orifice and approximation of the papillary muscles and their tendinous prolongations to an extent sufficient to allow of better closure of the orifice during systole. The right ventricle, if overburdened, is relieved, congestion on the venous side of the circulation is overcome, and the functions of various organs are bettered through the removal of stasis.

> If the writer's "digitalis test"—the giving of 25 drops of the French official

digitalin solution in every case of arterial or endocardial cardiopathy when compensation begins to fail—is negative, that is, if the heart does not show any tonic effect from it, other heart tonics are required,—strophanthus or sparteine. In case of transient trouble, with a resistant myocardium, the author gives large doses of digitalis followed by progressively smaller doses (constant effect). This is followed by a period of repose on a milk diet, returning to the digitalis in case of a new attack of heart weakness. In case of chronic trouble, with a degenerated or sclerotic myocardium, he commences with the digitalis test, and if the myocardium does not respond properly to the test he gives sparteine and strophanthus alternately for a week. When the heart has been steadied, he then gives the digitalis in a single large dose (25 to 50 drops in two doses), then follows with rest on a milk diet. Whenever the myocardium shows signs of wavering, then the heart tonics should be resumed first, and later the digitalin. The official digitalin to which he refers contains 1 mg. of active principle in 50 drops of the alcoholic solution. A case is cited to show how digitalis failed at first, but after the interposition of the heart tonics was able to exert its specific action and the patient was kept in comparatively good health by resumption of this alternate medication at need, with intervals of repose. Huchard (Presse méd., No. 1, 1905).

The best results of digitalis are obtained in cases of **mitral disease** associated with a deficient heart muscle. These results are probably due to an improved coronary circulation resulting in better nutrition to the heart muscle. Digitalis, on the other hand, fails in those cases in which the irregular and rapid heart action is due to nervous influences. Notable examples of this are paroxysmal tachycardia and the rapid pulse of Graves's disease. There are certain cases of extrasystole dependent upon organic changes that react very favorably to digitalis. However, when extrasystoles are the result of disturbances in conductivity, digitalis will usually fail. Edens (Therap. Monatshefte, Bd. xxv., Nu. 1, 1911).

Not infrequently the physician will be called when the patient is in acute distress, sitting bolt upright or standing bent over and struggling for breath, with marked nervous excitement, accelerated and irregular pulse, cold perspiration, possibly coughing and precordial pain. Under these conditions digitalis, while indicated, will not act promptly enough; the immediate requirements are for a hypodermic injection of morphine, guarded, if respiratory depression is feared, by a small dose of atropine or a larger one of strychnine. An injection of nitroglycerin, repeated, if need be, until intracranial pulsation is felt subjectively, or venesection, will often relieve the dilated heart and cut short the symptoms, though in cases where there is marked collapse and prostration ergot intramuscularly may be preferable. Once the attack is subdued digitalis should be given, either in the form of the tincture, in doses of 10 to 20 minims (0.6 to 0.12 c.c.) two or three times daily, German digitalin, ⅛ to ¼ grain (0.0075 to 0.015 Gm.), or the infusion, 1 to 3 drams (4 to 12 c.c.). In the final stage of mitral insufficiency Abrahams administers, to begin with, even a 1-dram (4 c.c.) dose of the tincture, to be repeated in twelve hours if there has been no satisfactory symptomatic betterment; the dose is then reduced to 30 minims (2 c.c.) three times a day, this being continued for the next two or three days, and finally to 20 minims (1.2 c.c.). In the less advanced cases the same author gives 10-minim (0.6 c.c.) doses for an indefinite period. Absolute rest is to be enjoined when large doses are being taken. It is also necessary to beware of toxic effects (see section on UNTOWARD EFFECTS), the fact being kept in mind that the drug is slowly eliminated and a summation of the action of successive doses occurs, with a tendency to renal vasoconstriction and further accumulation. Occasional intermission for a few days is advisable. Where prolonged administration is necessary, Whitla interrupts the digitalis every two months, and after a three-day rest gives strophanthus in smaller doses, with syrup of iron, quinine, and strychnine phosphates. Most clinicians intermit more frequently, *e.g.*, every two or three weeks, a ten-day rest being given.

It is often advisable, when beginning digitalis treatment, to prepare the ground for its action by preliminary catharsis and diuresis. The former effect may be secured, *e.g.*, by a full dose of compound jalap powder. A favorite procedure serving both cathartic and diuretic purposes is to combine the digitalis with squills and a mercurial, as in the so-called Guy, Addison, or Niemeyer pill:—

℞ *Pulveris digitalis,*	
Pulveris scillæ,	
Massæ hydrargyri...	āā gr. xxiv (1.5 Gm.).

Ft. pil. no. xxiv.
Sig.: One pill after each meal.

> The old Niemeyer pill, consisting of digitalis, squill and some form of mercury, is a good preparation and often produces excellent results. Its disadvantages are that the squill is apt to produce gastrointestinal irritation, and, unless carefully watched, the mercury may cause salivation. A. E. Taussig (Interstate Med. Jour., Aug., 1912).

Calomel might be used in place of the blue mass, acting more strongly, though at times less pleasantly for the patient. Huchard substituted powdered scammony for the mercurials, thereby relying solely on the squill for the direct diuretic effect, while Allbutt, in the presence of dropsy, combines the xanthin derivatives with digitalis:—

℞ *Theobrominæ sodiosalicylatis (diuretin)*	gr. x-xv (0.6-1 Gm.).
[*vel Theophyllinæ sodioacetatis (theocin sodium acetate)*	gr. iv (0.25 Gm.)].
Tincturæ digitalis..	♏v (0.3 c.c.).
Spiritus juniperi compositi	ʒss (2 c.c.).
Aquæ carui [vel anisi]	℥j (30 c.c.).

M. Sig.: For one dose.

Rest in bed and, in advanced cases, reduction of the intake of fluids are always to be remembered as powerful adjuvants to the favorable circulatory and renal effects of these drugs. Huchard limited the fluids in severe cases to 200 Gm. (⅖ pint) of a mixture of 3 parts of milk with 1 of water, four times daily. On and after the fourth day whole milk was substituted, but the quantity kept the same until the third week, when 1500 to 1800 Gm. (3 to 3½ pints) were allowed. Solid food was given only when the patient ceased losing weight.

> Patients with **cardiac dilatation,** whether the failure of the left heart is due to valvular diseases or to a primary myocarditis, should not be given digitalis when first seen. Instead the patient must be absolutely still in bed for at least twenty-four hours. Then digitalis can be given tentatively, in small amounts at first, gradually increasing the dose and feeling one's way with it until the proper degree of stimulation may be obtained. Some patients with primary myocarditis are distinctly harmed by digitalis. M. H. Fussell (Penna. Med. Jour., Nov., 1912).

The same author, and more recently Mayor, of Geneva, have advised the prophylactic administration of small doses of digitalis in heart cases, *i.e.*, the giving of the drug even during periods in which signs of insufficient cardiac function are but slight or absent. They consider it a mistake to leave off digitalis entirely when peripheral edema has disappeared. Huchard, in cases in which the myocardium is in the initial stages of degeneration, reduced the fluid intake for a short period every month or six weeks, and after this gave 1/650 grain (0.0001 Gm.) of the French "digitaline cristallisée" for ten days to two weeks. Attacks of heart weakness with peripheral edema can thus, according to this author, be put off or entirely prevented. Mayor, of Geneva, lays stress on the harm done to the various organs of the body, and hence to the system as a whole, by repeated attacks of heart weakness, and points out that if, after the first attack is passed, subsequent attacks are forestalled by periodic administration of small doses of digitalis, the general condition will be kept good much longer than would otherwise be the case and the ultimate serious circulatory breakdown materially retarded. The aim sought in giving small doses of digitalis, as advised by this author, is not to cause the heart to hypertrophy, but to maintain its ability to withstand temporary additional stresses, so that it will not at once become insufficient under the influence of emotional disturbances or when unusual muscular activity is indulged in. The condition to be established is the same as that seen in healthy individuals who take up mountain climbing in the spring, after being inactive all through the winter; on the first day, dyspnea and tachycardia are marked and out of proportion with the work performed, but on the second they diminish and on the third are no longer noticed, circulatory sufficiency having been re-established in spite of the fact that during the short period elapsed cardiac hypertrophy cannot have occurred. The object is thus not to allow a heart bearing a permanent lesion to lose the habit of performing the maximal amount of work of which it is capable, in order that when unusual stress comes the organ will not be exposed to dilatation. Sometimes this result can be secured by means of carefully supervised muscular exercises or through hydrotherapy; but in many instances these measures are not at all or only partially available, and in these, according to Mayor's experience, digitalis is of great assistance. Usually 0.3 Gm. (4½ grains) of digitalis, given in the course of three days three times in each month—on the 1st, 2d, and 3d, 11th, 12th, and 13th, and 21st, 22d, and 23d, of each month—is the amount required, though in some cases this may have to be increased to 0.45 Gm. (7 grains) or can be reduced to 0.2 Gm. (3 grains). The drug may be conveniently administered in the following form (Mayor):—

℞ *Fluidextracti digitalis,*
Fluidextracti hydrastis .... āā 4 Gm. (♏lxxv).
Glycerini .... 2 Gm. (♏xxx).—M.

Ten drops of this mixture, containing 4 drops (not minims) of the fluidextract of digitalis, are equivalent approximately to 0.1 Gm. (1½ grains) of powdered digitalis leaf. When through some accidental circumstance the patient becomes unduly fatigued, or in the event of any acute infection, even slight—bronchitis or influenza, for example—occurring, the dosage of digitalis should be temporarily increased. By proceeding in this manner, Mayor asserts, circulatory sufficiency can be maintained for so long a time as to afford the patient an illusion of complete health.

After a more or less prolonged period, however, heart weakness will begin to appear in the intervals between periods of digitalis administration. The next step which suggests itself is to increase gradually the total amount of digitalis taken in each three-day period from 0.3 Gm. to 0.35, 0.4, and even 0.6 Gm. (5 to 9½ grains). This may be tried, but often better results are obtained by reducing gradually the intervals between the periods of medication to seven, then to six, five, and four days. Finally, a time will come when circulatory equilibrium will hardly be maintained by digitalis for more than twenty-four hours. The drug treatment will then have to be continuous instead of interrupted.

Groedel, Kussmaul, Sahli, and Henrijean have reported cases of cardiac disease kept free from further attacks of failure of compensation for six, seven, and even twelve years by the daily ingestion of suitable doses of digitalis. One of Groedel's cases, after repeated attacks necessitating long periods of rest and increasing doses of digitalis, was kept free from any further attacks and enabled to resume and continue his work as a surgeon for eleven years by 0.05 Gm. (⅘ grain) of powdered digitalis leaves taken twice daily. In certain forms of **adhesive mediastinopericarditis** and of **aortic insufficiency** in arteriosclerotics, in cases where an idiopathic hypertrophy gives way to fibrous myocarditis with rapidly recurring acute decompensation, and in a few cases where the right heart is constantly menaced by reason of a chronic lung affection and the patient for some reason cannot be kept under watch, Mayor advises that the digitalis treatment be continuous from the first, and not begun with the intermittent form.

In continuous treatment the question of cumulative action has to be considered. Pouchet and Mayor agree, however, that 0.0001 Gm. (1/650 grain) of crystallized digitalin, *i.e.*, about 0.1 Gm. (1½ grains) of powdered digitalis leaves, does not exceed the amount that can be destroyed or eliminated daily by the adult human subject. If, with these small doses, signs of cumulative action should happen to appear (the patient being always instructed as to their nature) a single day's interruption would suffice, as a rule, to restore equilibrium. A second objection which might be raised to continuous treatment, viz., that a premature and excessive compensatory hypertrophy would take place, is shown to be groundless not only by the fact recognized by various authors, including Sahli, that life can be prolonged by continuous administration of digitalis (because the effects of stasis in various organs, which react unfavorably on the heart itself, are thus avoided), but also by the experimental work of Cloetta (1908), which showed that *therapeutic* doses of digitalis do not cause hypertrophy of the normal rabbit's heart; in rabbits in which aortic insufficiency had been artificially established, indeed, the drug was shown to render easier the work of the heart, for while among the animals not given digitalis the heart underwent hypertrophy to the extent of 80 per cent. and several succumbed to the cardiac disease, among those given therapeutic doses of digitalis the hypertrophy amounted only to 30 per cent. and none died until sacrificed for examination twelve to eighteen months after the production of the artificial lesion.

Report of cases showing the value of continuous administration of small doses of digitalis. One case was that of a woman 72 years of age, presenting dyspnea such that she was almost unable to walk, with cyanosis, marked stasis at the bases of the lungs, and murmurs at all the valves. Being placed upon digitalis, she took 620 powders each containing 1½ to 2¼ grains (0.1 to 0.15 Gm.) of the leaves. She was then taken with pneumonia, but continued the powders, and recovered. At the time of writing, over four years after the beginning of treatment, she had taken in all nearly 1200 doses. During this period she tried several times to leave off the remedy, but after a few days felt impelled to resume it. On one occasion, however, three years after the beginning of treatment, she left off the drug, upon request, for a month, and on this occasion bore the interruption of treatment better than she had been able to before. The use of the drug was only resumed in order to avoid the bad effects of cold, which she withstood better when under the influence of the drug. The pulse rate was from 82 to 90, and seemed hardly to have changed at all since the heart action had been made regular for the first time at the beginning of treatment. Henrijean (Bull. de l'Acad. roy. de Méd. de Belgique, vol. xxii, Nos. 3 and 4, 1908).

In mitral stenosis opinions concerning the value of digitalis are not unanimous as in the case of insufficiency of the same valve. The drug sometimes fails to yield the benefit expected of it. There seems to be no question, however, that when the right ventricle weakens, digitalis may do much good by toning it up. The objection has been raised that the drug may do harm by increasing the pressure and congestion in the lungs, but, after all, this could probably only occur if the beats of the right ventricle became stronger than they had been before this ventricle weakened. It is also possible for digitalis to do good by slowing the cardiac rate, thus allowing more time for the left ventricle to become filled through the narrow mitral orifice. At any rate, the administration of the drug in moderate doses may be tried when symptoms of circulatory insufficiency appear, and, if it fails to benefit or is not well borne, it can later be withdrawn and caffeine sodiobenzoate in doses of 5 grains (0.3 Gm.) tried instead. In the more advanced cases of mitral stenosis, complicated with regurgitation at the same orifice, there is no question of the efficacy of digitalis, which may be given in full doses. Where the patient begins to complain of dyspnea, Fiessinger gives 1/650 grain (0.0001 Gm.) of the French "digitaline cristallisée" daily for ten days, then reduces the dose to 1/930 grain (0.00007 Gm.) for ten days, and alternates thus until the symptom is completely relieved; finally ten-day periods with 1/650 grain (0.0001 Gm.) are alternated with like periods of complete intermission. The patient can thus very often be kept comfortable for a number of months.

In circulatory failure due to **mitral stenosis**, one should not only carefully weigh the import of the tumultuous cardiac sounds, but by the use of instruments of precision determine, if possible, whether there is delay in the transmission of the contraction impulse over His's bundle. If such a delay exists, digitalis in doses large enough to cause a distinct and sharp cardiac effect is probably capable of prolonging this delay and so doing harm. If given at all, the dose of digitalis must be so small as to produce a very gradual effect, one which will not consist in decreasing auricular contraction through vagal stimulation, but gently re-establish general cardiac power. At first one should give the patient absolute rest, unload the portal system by free purgation, use venesection to relieve stasis, and give rapidly acting diffusible stimulants for a few hours until the co-ordination of cardiac movement is re-established. When this is done, small doses of digitalis, arsenic, and iron may be used. Hare (Therap. Gaz., vol. xxvi, p. 244, 1910).

In cases of mitral stenosis with regular pulse, and those resulting from arterial disease, digitalis is often impotent or even harmful; the heart continues to dilate, and dropsy increases under its use. Windle (Brit. Med. Jour., Feb. 25, 1911).

In cases of mitral stenosis, digitalis is contraindicated if the presystolic murmur is missing, the jugular or liver-pulse is synchronous with the cardiac systole, and the heart occasionally skips a beat, with a tracing showing disturbance in conductivity. Martinet (Presse méd., July 8, 1911).

In **aortic insufficiency** it is, in general, the tonicity of the heart muscle that governs the administration of digitalis. Where, owing to insufficient coronary blood-supply, the muscle begins to dilate and the cardiac dullness shows enlargement greater than that corresponding to the primary excentric hypertrophy of the organ occasioned by the aortic leakage, the drug is in many instances capable of considerable benefit provided the dose is carefully adjusted. A seeming danger in these cases is that the cardiac rate may be unduly slowed by the drug, with resulting excessive prolongation of diastole, and hence—in this form of valvular disease—of the periods of blood stagnation in the vessels, the nerve-centers being meanwhile exposed to the evil effects of repeated temporary anemia. But by giving only small doses of digitalis the tonifying effect of the drug on the heart muscle can be obtained with relatively little change in the rate; upon cautious use digitalis can thus be made to do good where larger doses would do harm. Abrahams, for example, gives 5 minims (0.3 c.c.) of the tincture three times on the first day, 6 minims (0.35 c.c.) three times the second day, and continues to increase gradually until the desired effect is produced or the maximal dose of 20 minims (1.25 c.c.) three times a day is reached, when the initial dose is resumed and kept up indefinitely (preferably with an intermission of eight or ten days in each month). The patient should always be required to stay recumbent and be kept under rather close watch, so that the drug can be at once interrupted or the dose reduced if untoward symptoms should appear. It is recommended not to allow the pulse rate in these patients to fall below 80, in order to avoid anemia of the centers. The efficiency of atropine in abolishing vagal action where this is causing undue slowing of the heart rate is to be borne in mind. This drug may not only be used to exclude the vagi where syncopal phenomena appear, but given prophylactically with the digitalis to prevent too great a diminution of rate. In advanced cases of aortic regurgitation relative insufficiency of the mitral valve is likely to appear, the heart muscle having yielded to such a degree that the mitral leaflets can no longer come in contact across the orifice. Under these conditions digitalis is clearly indicated, though some caution in the dosage remains necessary, lest sudden cardiac failure should take place.

> The danger of giving digitalis in **aortic regurgitation** is entirely illusory. Sometimes, as in certain aortic lesions or in arteriocapillary sclerosis, it may be well to combine it with nitroglycerin or some other vasodilator, but even this precaution is usually unnecessary. A. E. Taussig (Interstate Med. Jour., Aug., 1912).
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> The old objection to digitalis in **aortic regurgitation** on the ground that prolongation of the diastole would allow an increased quantity of blood to pass back into the ventricle, is still held by some, but in the vast majority of cases it will be found that no slowing of the pulse is produced by the drug, while its action on the cardiac muscle may prove of great value. H. Hume Turnbull (Austral. Med. Jour., Oct. 19, 1912).
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> As soon as **aortic regurgitation** is accompanied by failing heart action, as shown by swelling about the ankles, pulmonary congestion, and other well-known signs, digitalis is the drug to be used. The same thing applies to **Adams-Stokes' disease:** When dropsy occurs, with enlargement of the liver, digitalis is indicated even if marked bradycardia is present. David Riesman (Penna. Med. Jour., Nov., 1912).

True, uncomplicated **aortic stenosis** is infrequent. Much oftener the condition is merely a roughening occurring in conjunction with more or less widespread angiosclerotic changes, and not infrequently combined with aortic leakage. In all forms compensation is likely to be maintained for a prolonged period, and no heart tonic will therefore be required. When the muscle finally gives way to dilatation, considerable myocardial fibrosis or degeneration will usually have occurred, particularly in aged patients, and moderation in the dosage of digitalis will consequently be indicated. Where, again, stenosis exists without pronounced myocardial disease, some authors contend that the free use of digitalis involves danger of vascular rupture, owing to the fact that the heart is greatly hypertrophied and will be aroused to powerful activity by the drug. On the whole, the point to be chiefly observed in using digitalis in aortic stenosis is thus moderation in dosage, except in the last stages. Relief of precordial discomfort will afford an indication as to whether the drug is proving of assistance to the heart or, on the contrary, is inciting it to excessive activity. Where the discomfort is increased, strychnine or caffeine may be substituted. In the earlier stages of aortic stenosis it may sometimes happen that the phenomena accompanying palpitation—the latter induced by some temporary emotional disturbance—are mistaken for heart-failure, and digitalis given; under these conditions the symptoms may be aggravated owing to the more or less marked muscular hypertrophy, and cardiac sedatives will be indicated instead.

In **tricuspid regurgitation**, a condition seldom uncombined and usually occurring as evidence of an overworked right ventricle owing to the presence of mitral leakage or obstruction in the pulmonary circulation, digitalis is generally not of the same striking degree of utility as in mitral insufficiency. While in the less severe uncomplicated cases it is capable of giving excellent results, a large proportion of patients with tricuspid insufficiency come under observation when cardiac enfeeblement is already far advanced, and the organ may fail to respond to digitalis as one might expect. In these refractory cases Fränkel recommends the intravenous administration of strophanthin. If it is not desired to resort to this extreme measure, digitalis in moderate doses, preferably in combination with theobromine or caffeine (A. Meyer), may be employed.

In 17 **mitral insufficiencies** with more or less compensation 15 reacted promptly and 2 with defective compensation negatively. In 4 cases of pure **mitral stenosis** 2 did not react; 1 was a case of hepatic stagnation, the other of dilatation and pulmonary infarction. In 31 with combined mitral insufficiency and mitral stenosis all reacted but 2, and in 1 of these there was severe myocarditis. Of 9 cases of **aortic insufficiency** digitalis was negative in 2, in 1 of which there was dilatation. When negative results could not be associated with cardiac conditions they could be traced to severe general or pulmonary affections. In several cases of association of tricuspid and mitral lesions the result was not significant, as there was as a rule dilatation of the right heart and stagnation of the liver. In 30 cases of associated aortic and mitral lesions the behavior under digitalis was very irregular, and there were at least 9 negative results in which various complications were accused. Of 33 affections of the myocardium, chiefly **chronic myocarditis**, there were 5 negative results which included 2 cases of goiter heart. In 5 cases of pericarditis with exudation, in which hepatic stasis coexisted, there was no reaction of any value. In nearly all the 21 cases of **cardiac insufficiency of chronic nephritis** (no manifest arteriosclerosis) the reactions were marked. In 13 cases with **arteriosclerosis** the results were good in 7. Here as elsewhere the increase of diuresis was one of the evidences of a positive reaction. Total failure generally argued a poor state of the cardiac muscle. Schrenk (Med. Record, from Münch. med. Woch., Dec. 31, 1912).

In **tricuspid stenosis** and in **pulmonary insufficiency** or **stenosis**, all infrequent lesions and usually congenital, the same considerations apply as in corresponding disorders of the left side of the heart, dilatation and weakening of the ventricular muscle constituting the chief indication for digitalis.

Cardiac Irregularity. — Relatively recent clinical studies, conducted with the aid of improved instruments such as the polygraph, have shown that the various forms of cardiac arrhythmia are reducible, according to their mode of production, to six fundamental types, viz., sinus arrhythmia, heart block, premature contractions, paroxysmal tachycardia, auricular fibrillation, and alternation of the pulse. Since these different forms present more or less definite and diverse indications in regard to digitalis therapy, it will be advantageous to discuss them individually. The subject as a whole, however, is one that cannot be divorced from organic heart lesions, and it is from considerations of simplicity and clearness alone that no mention was made of the arrhythmias in the preceding sections. Since each of the forms of irregularity can occur in association with a number of different organic or functional cardiac disturbances, it will be essential to state in every instance, as precisely as is now possible, the field covered by the arrhythmia under consideration.

Auricular fibrillation, according to Lewis the commonest of the arrhythmias, was formerly termed nodal rhythm by Mackenzie and represents one variety of what is frequently called the "permanently irregular pulse." The rhythmic stimulus which sets the heart in motion at each beat, normally developed at and propagated from the region of the sinus, *i.e.*, at the junction of the superior vena cava with the right auricle, is superseded in auricular fibrillation by the formation of abnormally frequent, irregular stimuli in the auricle, which not only result in loss of co-ordinate contraction in this chamber itself, but are transmitted in their haphazard succession to the ventricle. The latter, in turn, responds in so far as it can to the impulses received and contracts both at irregular intervals and with varying amplitude of beat. The rate is, as a rule, increased to 110 to 150. About one-half of all cases of this form of irregularity occur in mitral stenosis, almost one-fourth in myocardial degeneration, and the remainder in aortic disease, arterial disease and granular kidney. In nearly all hearts beating irregularly at a rate exceeding 120 the arrhythmia represents auricular fibrillation (Lewis). Constant irregularity, without intervening periods of regular rhythm, is characteristic. The symptoms are those of a failing heart muscle, sometimes with subjective sensations of precordial fluttering. In the less advanced cases of heart disease, however, attacks of fibrillation may occur at long intervals without giving rise to much disturbance. In general, auricular fibrillation is of unfavorable prognostic significance, few cases living longer than ten years after it has set in. The higher the heart rate the more serious the condition. It is in this type of irregularity, however, that digitalis is of greatest value. By impeding the transmission of the weaker impulses from the auricle to the ventricles, through diminished cardiac conductivity, the drug shields the ventricles from overwork by reducing their rate of contraction, and frequently produces a most striking improvement in the patient's condition. In the average case the tincture should be given in doses of 10 or 15 minims (0.6 to 1 c.c.) three or four times a day, the patient being meanwhile kept in bed. If a drop in the pulse rate should fail to occur in a few days, the dose may be increased until signs of intoxication occurs. In most instances, however, the rate will promptly fall, and when it reaches 60 to 80 the drug can be stopped, later to be resumed in doses of 5 minims (0.3 c.c.) if acceleration tends to recur when the patient rises from bed. In the most serious cases, with a rate of 170 to 200, strophanthin intravenously in the dose of 1⁄250 grain (0.00025 Gm.), repeated once or twice at bihourly intervals, may be substituted for large doses of digitalis (Lewis).

The total amount of tincture of digitalis required in **auricular fibrillation** to produce runs of coupled beats or regular slowing is, on the average, 450 minims (30 c.c.)—that is, in about ten days with doses of 15 minims (1 c.c.). Digitalis should be stopped when this occurs. Within two or three days the pulse quickens and is again characteristically irregular. The drug should now be given again in increasing doses of from 10 to 15 minims (0.6 to 1 c.c.) three times a day, until the pulse slows to a rate approximating that at which the double beats previously occurred; it is with this rate of pulse that the patient will generally be at his best.

Windle (Brit. Med. Jour., Feb. 25, 1911).

In the absence of instrumental aid, the following plan should be adopted in cases of **auricular fibrillation** in which extrasystoles are present and vitiating the true reading of the effect of digitalis: First count over the apex with a stethoscope the total beats during the space of a minute; then count for another minute the number of coupled beats heard. Finally subtract the number of these coupled beats from the total beats; the result indicates the degree of ventricular response to auricular stimuli, and consequently the degree of blocking effect of the drug employed. A much truer indication of the effect of the drug can thus be obtained, and a safer control effected. Lea (Med. Chronicle, May, 1912).

In **auricular fibrillation,** digitalis acts by impairing the conductivity of the bundle of His. If it is given in sufficiently large doses—and very large doses are required—the bundle becomes less and less able to transmit impulses from auricles to ventricles, and the latter, instead of responding to each considerable tremor of the former, contract only after the strongest ones. The result is a very marked slowing of the ventricular rate of contraction, much greater than in other cases of broken compensation, with all of the accompanying benefits to myocardium and circulation. If the digitalis be pushed unduly, a complete block of the bundle of His may result. The heart then beats very slowly, 30 to 40 times per minute and entirely regularly, with the exception, perhaps, of an occasional extrasystole. This complete heart block is usually only temporary, ceasing as soon as the digitalis is discontinued. A. E. Taussig (Interstate Med. Jour., Aug., 1912).

The most striking results of digitalis are seen in cases where the rhythm of the heart is given by the fibrillating auricle. But when **auricular fibrillation** is not accompanied by a rapid pulse, there is no very marked effect; improvement occurs but slowly. When, however, there is a very rapid irregular pulse, digitalis is followed by a rapid fall in the pulse rate and an improvement in all the symptoms. The slowing of the pulse may be used as a gauge of the action of the drug, and also as an indication as to whether the treatment should be continued. The slowing is not inhibitory in origin, for it remains after large doses of atropine. The auricle continues to fibrillate as before, and the digitalis may therefore be presumed to act either in the bundle of His or in the ventricle itself. Careful percussion in the author's cases failed to show any change in the limits of cardiac dullness in many cases in which obvious improvement in the symptoms occurred under treatment.

A dram (4 c.c.) of the tincture a day was first prescribed. This very often led to headache, nausea, or vomiting after a few days, or the pulse showed distinct effects; the drug was next abandoned for a few days, and then resumed with rather smaller doses. In many cases the best results were obtained at first only when the largest doses were taken which did not induce gastric symptoms. After a course of digitalis lasting for a fortnight or more, the patient often relapsed on giving up the drug. Renewed treatment restored the improvement, and finally a satisfactory condition could be maintained with comparatively small quantities or with larger amounts taken at intervals of several days. Since distinct improvement is rarely seen before the fourth day of treatment with digitalis, this precludes its use in the most acute cases. To elicit a more rapid effect the author injected strophanthin intravenously ($\frac{1}{250}$ to $\frac{1}{100}$ grain—0.00026 to 0.00065 Gm.) in a number of cases with most satisfactory results. Gibson (Brit. Med. Jour., Sept. 21, 1912).

Occasionally cases of **auricular fibrillation** are seen where the patient is not comfortable unless the dose of digitalis taken is large enough to maintain the coupled beats. In such cases the heart muscle is probably very badly affected, and no definite rule as to dose can be laid down. The physician must decide each case on its merits. It is important to remember that these small extra beats may not be palpable in the radial pulse, so that the physician may be deceived on feeling this, but they are easily recognized on auscultation. H. Hume Turnbull (Austral. Med. Jour., Oct. 19, 1912).

In **auricular fibrillation,** it is in the younger persons of the rheumatic group, especially if they have initial rapid pulse rate, that digitalis acts most successfully. In the non-rheumatic group (in which the persons are usually older) the results are not so encouraging. By the "atropine reaction" it is frequently demonstrated, especially in certain non-rheumatic fibrillating cases, that the slowing under digitalis is entirely vagal. The degeneration in the heart muscle in these cases seems to have reached a degree which renders it no longer capable of improvement. On the other hand, in the rheumatic group the atropine test proves the slowing is due to both vagal stimulation and cardiac tissue improvement. The latter being often much the larger factor, this shows that these hearts have a muscle capable of being helped.

When there is fibrillation, a patient with a pulse exceeding 100 while at rest needs digitalis. He should have 15 minims (1 c.c.) of the tincture or 1 to 2 drams (4 to 8 c.c.) of the fluidextract three or four times a day regularly, until the pulse slows to 70 or the physiological limit for digitalis is reached, as shown by headache, nausea, vertigo and possibly diarrhea. Not infrequently the first marked fall in pulse rate does not come until this physiological limit is reached. The drug should then be stopped. In some patients the pulse rate does not accelerate after the withdrawal of the drug, and there is little increase as the patients get up and around, until some new strain provokes a new attack. In a second group the pulse rate tends to accelerate after the digitalis is withdrawn, especially when the patients get up, but it can often be held in check by small doses, 5 minims (0.3 c.c.) two or three times daily. In a third group the larger doses of digitalis are necessary continually to keep the pulse rate in reasonable bounds. These are probably the patients where the entire slowing is due to vagal inhibition. Pronounced slowing is usually produced by 6 to 8 drams (24 to 32 c.c.) of digitalis, but where this fails it is often necessary to increase the doses to 20 or 30 minims (1.3 to 2 c.c.) three or four times a day.

If coupling of beats or any of the symptoms of the physiological limit appear, the drug should be stopped at once. Certain individuals cannot tolerate even small doses without some gastrointestinal disturbance. By such patients tincture of strophanthus or tincture of scilla in doses of 10 to 15 minims (0.6 to 1 c.c.) are better borne and may give the desired results.

In cases of fibrillation with the pulse running from 150 to 200, digitalis is too slow. The patients should have 20 to 30 minims (1.2 to 1.8 c.c.) three to four times a day, but first of all they should have strophanthin, 1/250 grain (0.00025 Gm.) intravenously every two hours, until the pulse rate is lowered. J. A. Talley (Penna. Med. Jour., Nov., 1912).

Premature contraction (extrasystole) refers to a condition of arrhythmia in which, with the heart beating normally a part of the time, there arise now and then, either in the auricles or ventricles, impulses peculiar in that they come too soon, a single premature beat of the heart thus taking place which is usually weaker than the normal beats owing to the fact that not enough time has elapsed since the preceding contraction for the heart to be thoroughly prepared for the next. The extra beat may or may not be felt at the wrist; in the latter event a long interval is noted between successive pulsations to which the term "intermittence" is commonly applied. Premature contractions occur in association with a large variety of disturbances, both cardiac and extracardiac, and of very diverse severity; they possess, therefore, but little direct prognostic significance. Among the organic cardiac disorders, they most frequently accompany myocardial degeneration, next aortic disease and mitral stenosis, and finally, in occasional instances, angina pectoris, Bright's disease, and arteriosclerosis. Associated in other cases are gastrointestinal disturbances with gaseous distention and indicanuria, pulmonary tuberculosis, toxic influences such as may depend upon the excessive use of tobacco or the caffeine beverages, or free administration of digitalis itself, and numerous other conditions. Extrasystoles are an evidence of excessive irritability of the heart, and frequently occur in individuals with neurotic tendencies.

In most cases the administration of digitalis is neither desirable nor useful, sedatives such as the bromides, with measures directed to the removal of the cause, being indicated.

> In primary **chronic myocarditis,** so-called, digitalis should not be used if there are extrasystoles, unless the heart has become incompetent, as shown by tachycardia, dilatation, dyspnea and the signs of passive congestion. The best results in broken compensation are obtained if digitalis is given in massive doses. A dram (4 c.c.) of the tincture daily is a moderate amount (divided doses). In about two days the maximum therapeutic effect will usually have been produced. The dose may then be cut in half. If the pulse becomes irregular, on account of the production of extrasystoles, too much has probably been given, when the drug must be discontinued for a time. After the severe symptoms of heart-failure have been overcome, tonic doses may be employed with advantage, as, for instance, 1½ grains of the powdered leaves or 20 to 25 minims (1.25 to 1.5 c.c.) of the tincture. A. E. Taussig (Interstate Med. Jour., Aug., 1912).

Sinus arrhythmia (pneumogastric arrhythmia, Satterthwaite) is a comparatively infrequent type of irregularity characterized by a periodic waxing and waning in the rate and amplitude of the heart beats, and is dependent upon the influence of overactive vagi, which at corresponding intervals cause changes in the activity of the sinoauricular node, or pacemaker of the heart. The disturbance is generally of no significance, and requires no special treatment. Digitalis in full doses may itself produce it.

Heart block is characterized in general by an abnormally low cardiac rate (bradycardia) and is an expression of diminished conducting power in the auriculoventricular bundle, a slender neuromuscular band of tissue through which the contractile impulse is conducted from the auricle to the ventricle. Heart block may be either partial, in which case a certain proportion of the ventricular beats fail to occur, but relationship of the others to the auricular beats is still preserved, or complete, when both the auricle and ventricle beat regularly but at entirely independent rates, that of the ventricle slower than in the case of the auricle. Dropped beats in heart block differ from extrasystoles in being completely lost to precordial auscultation, whereas most extrasystoles can be detected as feeble ventricular beats by this method; the jugular pulsations will, besides, be found, on inspection, more frequent than those palpable at the wrist. Many cases of heart block occur among the elderly, and the condition is usually an indication of more or less widespread cardiac or cardiovascular changes, especially those such as result from syphilis and rheumatism.

It may also be due to irritation of the vagus or vagi through compression by neoplasms at any part of their course, occur temporarily in various acute infections, and be induced by digitalis and allied drugs. In most instances vagal influences, including that excited by digitalis, only bring on heart block where the conducting power of the bundle of His is already impaired, but occasionally the condition can be induced without any previous disturbance (Josué and Godlewski). In any case, it is clear that digitalis is contraindicated in the presence of heart block, except if there be pronounced cardiac dilatation, when the drug may prove useful notwithstanding a further slowing in the rate; or where complete heart block already exists, when the rate of the ventricular beats may be actually increased by the drug. Care in dosage is, however, necessary, at least in the former variety of cases, as observations of Taussig have shown that by pushing digitalis where there is partial heart block, injury may be done to the already weakened bundle, a permanent complete block resulting and the patient's condition becoming worse.

Case of a man aged 48, who had steadily grown more dyspneic, and was confined to bed. Physical examination showed a dilated heart, a mitral leak, evidence of atheroma of the aortic valves, pulmonary edema, an engorged liver and great anasarca of the legs. The radial pulse was 82 per minute, every fourth or fifth beat dropping out. The sphygmogram showed a condition of partial **heart block**. The myocardial incompetence was so marked that digitalis seemed indicated in spite of the evidence of impaired conductivity; mistakenly, as soon appeared. He was given 15 minims (0.9 c.c.) of the tincture three times daily. On the third day, the pulse, which had been 80, dropped to 60, and then lower and lower until, in spite of the discontinuance of the digitalis, it reached 32 beats per minute. The diagram of the pulse rate shows that the digitalis effect was not produced until after the drug had been given forty-eight hours, but persisted for a week or more after its discontinuance. The sphygmogram usually showed complete dissociation of auricular and ventricular contractions, though occasionally every second auricular beat went through. The patient's condition meanwhile had grown subjectively much worse. Finally, he had a brief attack of faintness, suggesting a Stokes-Adams attack. He was taken off digitalis and put on theocin 5 grains (0.3 Gm.) *t. i. d.* A great polyuria set in, he grew rapidly better, the heart block again became partial, as shown by the sphygmogram, and the pulse rate rose to between 65 and 80.

It has been shown by Erlanger and Hirschfelder that heart block which is complete when the auricles are beating rapidly becomes less so if the auricles are slowed. If in such a case one gives large doses of digitalis, the auricles beat more slowly, the block becomes less complete, and the ventricles may beat more rapidly, if somewhat irregularly. A. E. Taussig (Interstate Med. Jour., Aug., 1912).

Paroxysmal tachycardia corresponds to the condition usually known as "cardiac palpitation," and consists essentially of a regular series of premature beats, all started at a single point in the heart, which point is generally other than the sinoauricular node, whence the contractile impulses normally arise (Lewis). The heart rate usually rises considerably above 100 per minute, and a characteristic feature is that the disturbance of rhythm occurs in attacks or paroxysms, which are of variable duration. The condition can probably not be said definitely to indicate cardiac disease, for in most instances no sign of a valvular lesion can be found. In some patients, however, a tendency to dilatation of the heart and dyspnea on exertion is noted. The valvular lesion most frequently accompanied by paroxysmal tachycardia is mitral stenosis. Emotional stresses or exertion, acute illness, overeating; indulgence in coffee, tea, or alcohol; digestive disturbances, and the assumption of certain positions are the commonest determining causes of paroxysms. In some cases, however, no exciting factor can be found in association with the attacks. For their relief, digitalis is only occasionally of service, and it is not possible to tell in which cases it will prove useful. A single full dose may arrest the paroxysm, but frequently the assumption of a certain posture—known to the patient alone—an ice-bag over the precordium, emesis or the relief of flatulence, and the administration of bromides or morphine are more effectual. Vaquez advises that where, in spite of appropriate measures, a paroxysm continues more than three or four days and signs of serious heart weakness appear, 1/128 grain (0.0005 Gm.) of amorphous strophanthin be injected intramuscularly, on the next day, if necessary, 1/64 grain (0.001 Gm.) by the same route, and on the third day, if required, the last-named dose intravenously. In treatment during the intervals, the utility of digitalis seems largely limited to cases where evident cardiac disease is present, though Lewis states, without referring in particular to these cases, that a full course of digitalis (at first pushed until symptoms appear) may ultimately bring about improvement, and Carnot and Baufle have reported a case in which continuous administration of small doses gave good results.

> In 2 cases of **tachycardia**, the beats arising from an abnormal point in the heart, digitalis caused return to a normal rhythm, first inducing fibrillation of the auricle. Mackenzie (Heart, vol. ii, 273, 1911).

To be distinguished from the relatively infrequent cases of true paroxysmal tachycardia are numerous instances also commonly labelled "palpitations" in which an excessive heart rate is more continually present, as in the "irritable heart" of neurotic patients, athletes, or soldiers; tobacco, coffee, tea, or alcohol addicts, and mentally overworked individuals. Here the subjective sensation of a strongly beating heart is usually more pronounced than in paroxysmal tachycardia, but simple measures are more likely to bring relief where there is distress and the removal of the cause is usually more or less easily accomplished. Digitalis is generally inappropriate and unnecessary, unless the heart is weak. The same is true in the case of tachycardia induced by excessive thyroid activity, as in exophthalmic goiter, and in infections such as tuberculosis. On the other hand, in the "palpitation" experienced where the heart is acutely dilated owing to overexertion, digitalis is highly efficient.

Alternation of the pulse, the sixth and last distinct form of arrhythmia, consists in a succession of beats regular as to time, but in which alternate beats show a constant difference in size. It occurs (1) as an accompaniment of paroxysmal tachycardia, when it is of but slight importance; (2) in cases of angina pectoris, high arterial pressure, renal disease and fibrous myocarditis (Lewis), when it is of distinctly unfavorable prognostic significance, signifying that the heart is overburdened and cannot long hold out, and (3) occasionally as a sign of digitalis intoxication. The alternation is generally but slightly marked and detectable only by sphygmography, though even under these circumstances it loses none of its evil portent when associated with organic cardiovascular-renal disease. The chief desideratum in these cases is less work for the heart, and hence, primarily, physical quiet and removal of factors tending toward mental excitement. The indications for digitalis vary and cannot be definitely stated. While a number of authors have observed the appearance or accentuation of pulsus alternans upon administration of digitalis, Wenckebach has seen the drug remove this form of irregularity in several patients, to the extent that even active exercise failed to cause it to return.

In true **angina pectoris**, associated with coronary disease or aortitis, digitalis is contraindicated. In angina accompanying myocarditis, however, Fiessinger asserts that digitalis in very small doses in conjunction with theobromine (considered a coronary vasodilator) may sometimes do good, though rest in bed is, in general, the best measure of all for relieving the pain. Where the condition is encountered in interstitial nephritis, the same combination (digitalis in small amounts only), together with the dietetic and eliminatory measures appropriate in this affection, will nearly constantly bring about improvement. Meyer points out the fact that in the presence of mild degrees of cardiac insufficiency the result of myocarditis, mere extrasystoles and slight hepatic stasis may be the cause of angina. Under these circumstances small doses of digitalis may prove promptly effectual. In angina pectoris without evidence of insufficiency, on the other hand, digitalis may do positive harm; diuretin (theobromine sodium salicylate) in full doses should be administered instead. In the so-called "pseudoanginas," in which pain is referred to the heart in the presence of digestive disturbances, gall-stones, left-sided dry pleurisy, intercostal neuralgia, etc., digitalis is, of course, contraindicated unless evidences of poor circulation coexist, when small doses of the drug may prove useful.

In **acute pericarditis** digitalis is not of value unless there are indications of a tendency to heart-failure. When it is given, close observation of its effects is necessary, lest the increased amplitude of beat occasioned by digitalis be unduly hampered by the pericardial effusion, and the drug, owing to the slowed heart rate, therefore diminish instead of increasing the output of the heart. Where the right ventricle becomes dilated in pericarditis, Brunton considers diuretin more useful than digitalis. In **chronic adhesive pericarditis**, the drug is occasionally productive of good results in cases where marked myocardial changes do not as yet exist. When progressive cardiac insufficiency is encountered, however, digitalis is less effective than where the phenomena of stasis arise from causes other than adhesive pericarditis (Kovács).

As Circulatory Stimulant in Emergencies.—Although digitalis is especially suited for use in chronic disorders of the heart, its powerful exciting and tonifying effect on the myocardium and stimulant action on the vasomotor center also render it valuable for the treatment of acute circulatory depression, as in **collapse** under anesthesia, **shock** due to a variety of causes, severe **ptomaine poisoning, mushroom poisoning,** and poisoning by circulatory depressants such as **aconite,** or, in fact, by any drug which in the later stages of its effects brings about the same condition, *e.g.,* **acetanilide, alcohol, chloral hydrate,** etc. In all these conditions the relative slowness of action of digitalis should be remembered, more quickly acting agents, such as ammonium compounds, ether, caffeine or coffee, strychnine, atropine, and saline infusion or hypodermoclysis being administered at the same time as the digitalis in order to sustain the circulatory functions until the foxglove begins to take effect. The methods of giving digitalis in these cases have already been referred to. (See MODES OF ADMINISTRATION.)

Miscellaneous Other Conditions.—Digitalis has been recommended in a number of affections not essentially circulatory in nature. Its effects in most of them are of a far less certain and striking character than in the disorders already discussed, and are not explainable on the basis of our present knowledge of digitalis pharmacodynamics, except in so far as the action on the circulation may participate in any benefit produced.

> Stress laid on the continuous administration of digitalin in the nutritional disturbances of senility. The author has seen otherwise failing treatment converted into success by the addition of digitalis in cases of **ununited fracture, ulcers, edema, effusions,** and the albuminuria due to passive hyperemia. Senile **vesical paralysis,** with its necessary accompaniment, catheterization, may be overcome by prolonged use of digitalis. Beates (Monthly Cyclo. and Med. Bull., Sept., 1912).

Thus in **pneumonia,** both **lobar** and **lobular,** a number of authors have maintained that digitalis exerts a favorable effect, the mortality, indeed, being reduced according to Petresco, Fickl, and Bloch. Frequently repeated doses of a strong infusion were formerly advocated by adherents of the "specific" digitalis method. Barth gave as much as 45 grains (3 Gm.) of the powdered leaves a day, exhibiting it every two hours in an infusion with rum and syrup of orange-peel. Slight vomiting and vertigo were not considered contraindications, though an abnormally slow or an irregular pulse were taken to indicate discontinuance of the remedy. More recent experience with the remedy has shown that digitalis exerts no special beneficial effect in relation to the disease process, though it is not infrequently useful where the heart action becomes feeble owing to the excess of work imposed upon this organ. In general, fever markedly diminishes the efficiency of digitalis; this drawback may sometimes be overcome by the simultaneous application of an ice-bag over the heart.

> In **pneumonia** the heart often responds beautifully to digitalis, and indeed it may be well to give it, in moderate doses, from the beginning of the illness. Here the heart-failure may be due not so much to the toxemia as to the obstruction to the lesser circulation induced by the massive consolidation of the lungs. There is thus a relatively unimpaired heart, struggling under an unusual load, and one may rationally expect it to respond to stimulation. When the heart-failure is due to toxemia, digitalis is quite as ineffective in pneumonia as in other infections.

A. E. Taussig (Interstate Med. Jour., Aug., 1912).

The **cardiac insufficiency** which comes from long-continued fever, from septic infection, etc., is but little helped by digitalis, though certain cases appear to better from its use.

The heart in **pneumonia** at the acme of the disease frequently begins to dilate and sometimes to intermit—one of the most formidable of symptoms. Herè digitalis, hypodermically, occasionally will tide the case over to safety. M. H. Fussell (Penna. Med. Jour., Nov., 1912).

In various other infections, *e.g.*, **typhoid fever, diphtheria, septicemia** and **pyemia, plague,** etc., similar considerations apply. The drug should not be used empirically, but for the specific purpose of overcoming circulatory weakness. Due caution should be exercised in the initial dosage, for where the myocardium is the seat of acute degeneration large amounts may prove harmful. Some observers consider strophanthus more effective than digitalis in the presence of fever.

In the acute infections, the action of digitalis on the heart muscle is counteracted by the pyrexia, by the depressing action of the toxins upon the heart muscle, and by the often associated vasomotor paresis affecting chiefly the vessels in the splanchnic area. But in many cases it can be employed with advantage, although the results obtained are often not very manifest. Caffeine and camphor appear to have a more definite action. A. D. Blackader (Therap. Gaz., Oct., 1908).

Upon the heart seriously impaired by **typhoid** infection digitalis exerts a favorable and frequently a directly life-saving influence. In severe cases a combination of digitalis with small doses of ether, as recommended by von Jaksch, is indicated for the purpose of securing a more rapid action. Hemorrhage from the bowel is not an absolute contraindication to digitalis treatment. In marked collapse, where a more prompt effect is required, camphor, caffeine, etc., are to be preferred. A. Skutetzky (Med. Klinik, No. 22, 1911).

Other conditions in which the use of digitalis has been advised, seemingly with less justification, include **hydrocephalus, epilepsy,** the **insanities, hemoptysis, bronchial asthma,** and **spermatorrhea.** It has also been considered helpful in the reduction of **incarcerated hernia** and for the prevention of **abscess** formation.

Digitalis used to arrest the tendency to spontaneous **epistaxis** in 84 cases. In 75 per cent. of the patients the tendency to nose-bleed was promptly and permanently arrested within twenty-four hours after taking the digitalis, even in a few cases in which the bleeding was due to some anatomical abnormality, correction of which later permanently arrested the tendency. Focke (Therap. d. Gegenw., Sept., 1910).

Hemorrhage from the lungs is not due to tuberculosis in as large a proportion of cases as is generally assumed. Among the most important other causes are **anemia, arteriosclerosis, bronchial asthma,** and **acute catarrhal bronchitis.** In these conditions the **hemorrhage** occurs almost invariably from local congestion, inducing diapedesis. As the diapedesis occurs only from local stasis, treatment should aim to regulate the circulation in the region, and for this nothing is so effectual as digitalis. The proper measures are diet, keeping the bowels open and regulating the circulation with digitalis. The author generally orders for adults an infusion of the leaves. An accurate diagnosis of the condition causing the hemorrhage is necessary before the treatment is instituted. Focke (Therap. d. Gegenwart, Bd. lii, S. 306, 1911).

Large doses of digitalis are often tolerated by alcoholics, in particular those suffering from **delirium tremens.** In the latter state the not infrequent beneficial effect of the drug on the general condition, including that on the delirium, appears to depend largely on the improvement in the circulatory functions.

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and
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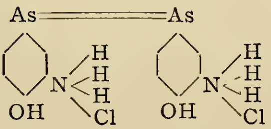
DILATATION OF THE HEART. See Heart.

DIMETHYLAMIDO-ANTIPYRIN. See Pyramidon.

DIONIN. See Opium.

DIOXYDIAMIDOARSENOBENZOL (salvarsan; arsenobenzol; 606) is an organic compound of arsenic prepared by Bertheim, biologically tested in animals by Hata, and introduced into medicine in 1910 by Ehrlich, under whose direction the synthesis and experimental investigation of a long series of arsenical substances had been conducted. Dioxydiamidoarsenobenzol was in reality number 605 in this series; the compound dissolved in water, however, only with great difficulty, and it was therefore converted to the hydrochloride, *i.e.*, dioxydiamidoarsenobenzol dihydrochloride, or 606, the molecular formula of which is $C_{12}H_{12}N_2O_2As_2.2HCl$, and the graphic formula:—



In addition, for each molecule of the compound there are present, in salvarsan as commercially supplied, two molecules of water.

Dioxydiamidoarsenobenzol hydrochloride occurs as a fine, yellow powder, soluble in water, in methyl alcohol and in glycerin, less easily soluble in ethyl alcohol (1 part in 12), and insoluble in ether. When placed in water, the drug at first clumps together; shaking the mixture with glass beads is therefore a useful procedure to accelerate dissolution. The resulting solution is acid in reaction. Before it is used sodium hydroxide is added to it to an extent sufficient to render it feebly alkaline. From this solution carbon dioxide precipitates the salvarsan; this is the reason salvarsan solutions gradually become turbid when exposed to the air.

Salvarsan, moreover, even in solid form, easily becomes oxidized when in contact with the air for any length of time; the resulting substance is an oxide in which the two portions of the salvarsan molecule are split asunder, the two mutual bonds of affinity between the arsenic atoms being now satisfied by oxygen. This oxide is about twenty times as toxic as salvarsan; a good preparation of the latter should not contain more than 0.5 to 0.8 per cent. of the oxide (Ehrlich and Bertheim).

Neodioxydiamidoarsenobenzol (neosalvarsan; 914), introduced by Ehrlich in the latter part of the year 1911, is chemically a condensation product of salvarsan and formaldehyde sulphoxylate of sodium ($H_2C.OH.OSONa$), and may be represented graphically by replacing one of the hydrogen atoms united to nitrogen in the above formula by the group $CH_2.OSONa$. This preparation has the pronounced advantages of dissolving at once when dropped in water and of yielding a neutral solution, so that the addition of sodium hydrate for purposes of neutralizing is unnecessary. Neosalvarsan contains only 21 per cent. of arsenic, while salvarsan contains 31 per cent.

Curves published by Ehrlich show that whereas the toxicity of a solution of salvarsan is increased two and one-half times upon exposure to the air for six hours, the same increase occurs in the case of neosalvarsan in but one-half hour.

> Experiments in mice, rabbits, fowls, and pigeons showing that whereas neosalvarsan is much less toxic than salvarsan when administered intravenously, when the drugs are injected subcutaneously salvarsan is less toxic than neosalvarsan.
>
> When neosalvarsan is injected either subcutaneously or intramuscularly it is more rapidly oxidized in the tissues than salvarsan, and in consequence is more toxic. It is evident, therefore, that the intravenous method is the only one suitable in the use of neosalvarsan. The curative action of the latter on rabbit syphilis is twice as great as that of salvarsan and in other spirochetal infections the difference in the curative action is equally well shown. G. Castelli (Zeit. f. Chemotherapie, I. Teil. Orig., vol. i, No. 3, 1912).

DOSE.—The dose of salvarsan for adults ranges from 0.2 to 0.6 Gm., the latter amount being the average full dose for a male subject, and the former used where dangerous complications are feared. The average full dose for female subjects is 0.5 Gm. The patient's general condition and the information obtained by physical examination should be taken into account in deciding upon the dose, the fact being borne in mind, however, that the largest dose that can be administered without doing harm will, under most circumstances, give the best therapeutic results.

> Care as to dosage particularly necessary in patients with nervous symptoms and in the early secondary stage of syphilis where it is likely that the meninges also harbor large numbers of the germs. Thus where there is the slightest suspicion of an involvement of the central nervous system, the initial dose should not exceed 0.15 to 0.2 Gm. Care is also required in anemia and in affections of the lungs. During the intervals between the injections, the patients should receive mercury in some form. In many cases it is desirable first to treat the patients with mercury so as to remove a large percentage of the invading germs before the more potent neosalvarsan is injected. The neosalvarsan should be dissolved in 0.4 per cent. saline solution instead of plain distilled water, and treatment should be persisted in as long as the seroreaction is positive. The author formerly gave three intravenous doses of 0.3 to 0.5 Gm. of neosalvarsan with one day between each injection, but has recently seen toxic effects, generally in the form of an eruption. Since a cumulative effect seems to be present it is better to wait longer before repeating the injection. E. Schreiber (Münch. med. Woch., Aug. 20, 1912).
>
> The dosage of salvarsan is as much as can be taken with the patient feeling as well or better than he did at the beginning of treatment, enjoying his food and not losing weight. Edward Martin (Penna. Med. Jour., Nov., 1912).
>
> Total of 2147 injections given to 1000 patients. There was invaliding in only 13, no deaths, and only 24 clinical relapses. The relapses were chiefly among those who had received not more than 2 injections, while of 68 cases in which 3 injections had been administered, there was a relapse in only 1. Lancelot Kilroy (Lancet, Feb. 1, 1913).

The dose of neosalvarsan is one and one-half times that of salvarsan.

MODES OF ADMINISTRATION.—The intravenous intramuscular, subcutaneous, and rectal routes have all been employed in giving salvarsan. The first of these was soon found to be the best of all, and since it is that generally employed it will be described first. The subcutaneous method proved very unsatisfactory, and has been abandoned. The rectal method is of service in a limited number of cases. In infantile syphilitic cases milk, both maternal and from the lower animals, has been used as a vehicle for salvarsan. In local diseases, mostly non-syphilitic, the drug is not infrequently applied externally.

Intravenous Method.—As already stated, salvarsan as such forms a strongly acid solution, owing to the hydrochloric acid it embodies. This reaction must be changed before the compound is administered. The usual mode of procedure is as follows: About 30 to 40 c.c. of sterile physiological saline solution (0.9 per cent.), made from C. P. (chemically pure) sodium chloride and freshly distilled water, are placed in a sterile graduated cylinder of 500 c.c. capacity. The graduate should preferably be provided with a ground-glass stopper, and may contain about 50 sterile glass beads, to facilitate dissolution of the salvarsan by shaking. The required dose of the drug is then dropped in and the graduate agitated until the compound enters into solution. Neutralization is next effected by adding a 15 per cent. solution of pure sodium hydroxide in a certain specified amount, which varies according to the dose of salvarsan used, as may be seen in the following table:—

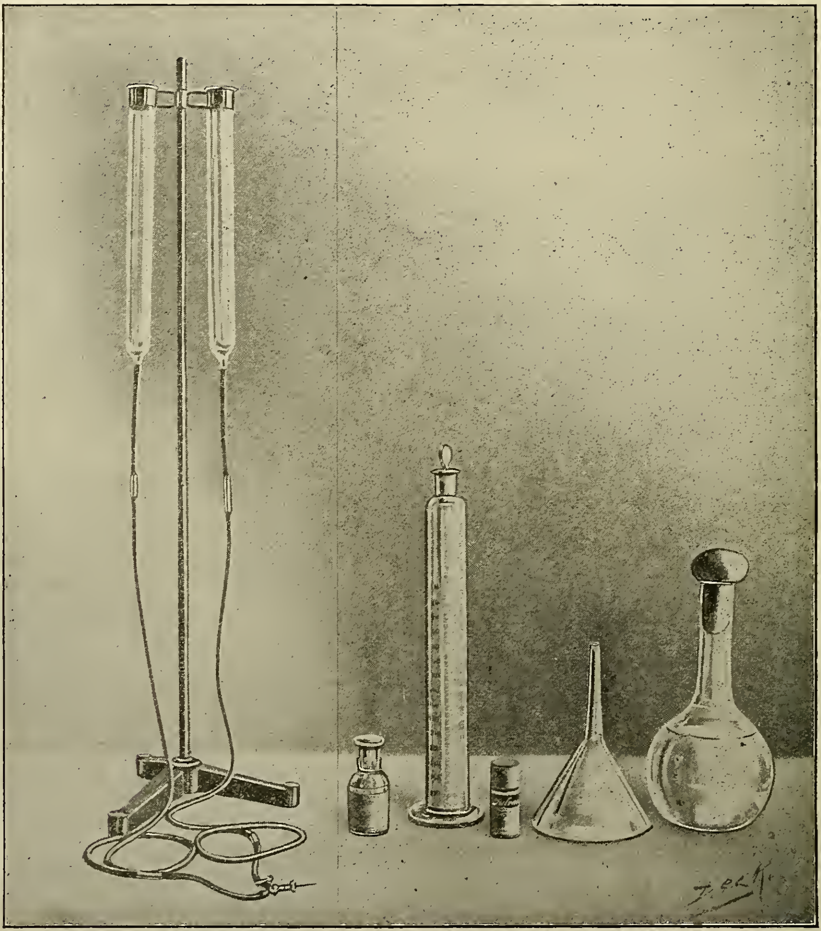
Dose of salvarsan.	Volume of alkaline solution to be added.
0.6 Gm.	1.14 c.c. = 23 drops.
0.5 Gm.	0.95 c.c. = 19 drops.
0.4 Gm.	0.76 c.c. = 15 drops.
0.3 Gm.	0.57 c.c. = 12 drops.
0.2 Gm.	0.38 c.c. = 8 drops.

The addition of the sodium hydroxide leads to the formation of a precipitate, which redissolves, however, upon vigorous shaking. Enough saline solution is then added to make as many times 50 c.c. (or 40 c.c.) as there are tenths of a gram (0.1 Gm.) in the dose employed. Thus, if a 0.5-Gm. dose were being used, the solution would measure 250 c.c. (or 200 c.c.). The finished preparation should be absolutely clear; if it is not, a few drops more of the sodium hydroxide solution should be added.

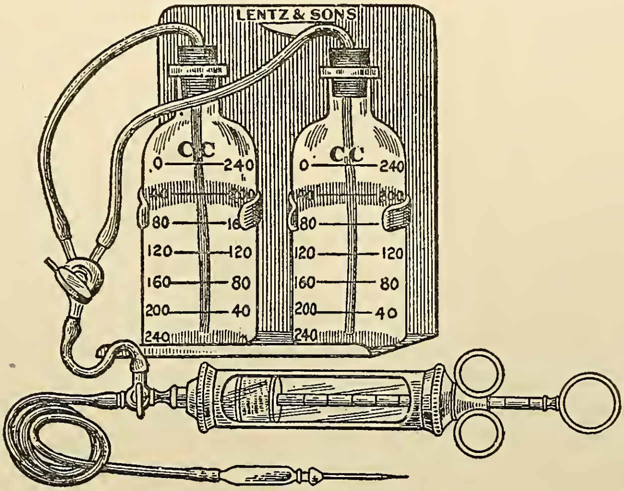
> Water is used in place of normal saline because it has been noted that upon the addition of saline there was a flocking out of the salvarsan, which it sometimes is impossible to redissolve with sodium hydrate. This inability always to obtain a clear solution with saline has been noted by many workers. While the solution with water is somewhat hypotonic, it is not hemolytic when mixed with blood-serum and cells, and careful observations of the urine after its injection have failed to show any hemoglobinuria. Furthermore, in test-tubes a mixture of alkaline sodium chloride solution of salvarsan with blood-serum gives a precipitate much sooner and in much higher dilution than a similar alkaline solution of salvarsan dissolved in water.
>
> An acid solution has been used intravenously, but it is attended with great danger. H. F. Swift (N. Y. State Jour. of Med., June, 1911).
>
> Physiological salt solution (250 c.c.—½ pint) without medicinal admixture produces temperature elevation. Simple distilled water should, therefore, be preferred to normal salt solution. Stümpke (Deut. med. Woch., Jan. 25, 1912).

The solution may also be prepared by placing the salvarsan in a small sterile mortar, dropping the required number of drops of 15 per cent. sodium hydrate solution directly on to the powder from a sterile pipette, triturating the powder and alkali with a sterile pestle or a thick glass rod with rounded ends, and pouring the resulting clear-yellow solution into a larger sterile receptacle containing the required number of cubic centimeters of sterile physiological salt solution (*e.g.*, 250 c.c. for a 0.5-Gm. dose).

In administering the injection nothing more complicated is essential in the way of apparatus than a graduated 300-c.c. burette or even a funnel to the lower end of which is attached a piece of rubber tubing, closed below by a clamp and leading to a stout hypodermic needle. The receptacle is hung or held at some elevation above the patient and the solution allowed slowly to run into the vessel. An advantageous variation from this, however, consists in the employment of two burettes or other receptacles, one for the salvarsan solution and the other for pure normal saline solution; the two tubes leading from these receptacles join in a three-way stopcock, which permits of running into the vein either salt solution or salvarsan at will.


Assmy's apparatus for intravenous injection of salvarsan.

Some surgeons, Schreiber in particular, employ a large syringe. A more frequently used form of apparatus, however, is one similar to that shown in the annexed illustration, in which a three-way stop-cock is connected with the nozzle of a 20 or 50 c.c. Record or other glass and metal syringe. One of the rubber tubes attached to the two distal openings of the cock leads to the needle, while the other is connected with salvarsan solution and saline solution receptacles, or is left free so that its extremity can be dipped at will in either receptacle. The tube leading to the needle should be interrupted with a "window" of glass tubing or some other arrangement made so that any air-bubbles in the tubing may be seen before they can enter the vein. The syringe is first filled with saline solution and this injected, next the cock is turned so that the syringe can be filled with salvarsan solution, and successive syringefuls of the latter are injected until the dose to be given is exhausted, after which another syringeful of pure saline solution is drawn in and injected.



Apparatus for injection of salvarsan. The glass handle, connected with the needle through a slip-joint, acts as a guide in the insertion of the needle and receives the blood when the vein has been entered. (*Cary.*)

For the intravenous method the author employs the Lüer syringe, using only 10 c.c. of sterile salt solution and mixing the doses in a mortar. He has used as little as 5 c.c. with no untoward results, and favors the reduction to a minimum of the bulk of fluid injected. As soon as the solution clears under the addition of 15 per cent. sodium hydrate, drop by drop, the fluid is filtered and injected. The rapid flow of blood in the vein dilutes the drug so thoroughly, if it is slowly injected, that it is absolutely shorn of all irritating properties. G. F. Lydston (N. Y. Med. Jour., Oct. 21, 1911).

Bernard has described a simple apparatus in which the force propelling the solution into the vein is obtained through compression of air, the device consisting essentially of a closed receptacle and a double-valved atomizer bulb. The container consists of a wide-mouthed bottle of 12-ounce (360 c.c.) capacity, provided with a rubber stopper through which two glass tubes are passed, one reaching to the bottom of the bottle and the other, with which the bulb is connected, merely passing through the stopper. After preparation of the solution the latter is filtered into the bottle, which is meanwhile placed in hot water, to warm the solution as it drops in. In using the apparatus the first step is to remove all the air from the tubing by holding the latter vertically and compressing the bulb until a solid stream of fluid passes out through the needle. The tubing is then clamped and the needle inserted into the patient's vein, when the clamp is loosened and the fluid from the graduated bottle introduced into the circulation by pressure on the bulb.

Uhle and McKinney have devised an apparatus designated as the "vacuum burette." The burette is double-walled, and between the two walls is a vacuum which prevents loss of heat from the fluid placed in the inner lumen. Near the lower end of the rubber tubing attached to the reservoir is a thermometer. The needle used is of platino-iridium. The salvarsan is prepared by dissolution in 30 c.c. of normal saline solution at 118° F., neutralization being effected by the addition of 15 per cent. sodium hydrate solution drop by drop until the compound has been fully precipitated and redissolved. After running saline solution into the vein, the salvarsan solution is poured into the burette, and when it has passed into the circulation the receptacle and tubing are flushed with 10 c.c. of saline solution (Loux).

The vein into which the injection is made is either the median cephalic, median basilic, or the anterior radial or ulnar vein—usually the first of these. The skin is first washed with green soap and water, then with sterile water and finally with alcohol. Some surgeons, after the cleansing with soap, lather and shave the part, apply tincture of iodine, wash this off with alcohol, then apply ether. A towel tourniquet or a bandage is next placed three or four inches above the elbow, in such a manner that it can be quickly undone, sterile towels clipped round the patient's arm, a prominent vein chosen, and the needle—a large one, preferably of platinum—passed directly through the skin into the distended vein. (In stout individuals or in children with small veins, the making of an incision or small V-shaped flap under local anesthesia and passage of the needle or a small cannula into the exposed vessel are sometimes necessary.) If the point is not in the vein, having either failed to penetrate or passed entirely through it, injection of a small amount of saline solution will at once cause visible infiltration and a slight swelling. If the needle has entered the lumen, on the other hand, blood will drop from it; or, if a syringe is being used, a little blood may be drawn out to make sure of the entrance, then immediately reinjected. (Occasionally a cannula, with trocar, is used instead of the needle, the trocar being withdrawn after the cannula has been introduced and the tubing from the salvarsan receptacle then attached, due care being taken to avoid the introduction of air; or, the needle attached to the tube may be fitted to the cannula, so that it can be slipped into it.)

Both indirect and direct administration should be employed whenever possible. Employing the intravenous route of administration in children, it will usually be found easiest to expose the vein before attempting to insert the needle. The dosage should be not less than 0.01 Gm. per kilogram of body weight. Repeated injections and supplemental treatment by mercurials may be necessary. The Wassermann reaction should be followed for a year. La Fétra (Archives of Pediatrics, Sept., 1912).

With the needle in position in the vein, it can be maintained there by a piece of gauze, tied around the rubber tubing and arm just above the needle. The tourniquet is next removed from the arm and some salt solution, at the proper temperature, allowed to run into the vein to make sure that no fluid will leak into the surrounding tissues. This precaution having been taken, the salvarsan solution is started. The patient meanwhile is recumbent. The injection of salvarsan should occupy five to ten minutes, and be interrupted for two or three seconds each minute (Martin). When it is concluded, sterile salt solution to the extent of 75 to 100 c.c. should be run in to wash all trace of the arsenic compound from the vein at the seat of injection, thus avoiding subsequent local irritation.

Do not infuse the solution into the vein too rapidly. It is best to have a needle of such capacity as will take eight minutes to introduce 200 c.c. of fluid. With the gravity apparatus the rapidity of inflow can be readily governed. Do not use glass pearls in the mixing jar, as small parts may chip off and cause embolism. Do not use a routine dosage of the drug, but gauge it according to the weight of the patient and the condition to be treated. Do not persist in intravenous injection if the patient shows signs of collapse during administration, but stop at once. J. F. Schamberg and N. Ginsburg (Jour. Amer. Med. Assoc., Feb. 4, 1911).

Schreiber advises that if, during the injection of the salvarsan solution, leakage should occur, the skin becoming lifted up and the patient complaining of a burning sensation, a certain amount of bleeding should be allowed, as he has found this the best way to avoid infiltration of the tissues. Where the injection is completely successful the patient should experience no pain except that due to the small skin wound.

After the needle or cannula is removed, the patient's arm should be elevated and sterile gauze previously dipped in alcohol applied to arrest the bleeding. Collodion may then be applied to seal the wound, and a dressing of gauze, fixed with adhesive, terminates the procedure.

All apparatus should be sterile before use. Receptacles open at the top may be covered, before sterilization, with four or six layers of gauze, through which the sterile solutions may be poured into the receptacles immediately after these have been removed from the boiling water or autoclave. Burettes and similar receptacles may be sterilized instead with formaldehyde solution, followed by sterile water and alcohol.

The flask containing the sterilized distilled water for use in making the solutions should not be stoppered with cotton, but with gauze, as cotton fibers, falling into the fluid, might cause trouble. The best syringe for injecting is a glass Lüer of about 20-c.c. capacity. It should not have a metal plunger, as in that case the least blood may cause binding. Schreiber has a special needle made with a bayonet bend in the shaft, and on this bend a ribbed finger-hold, The bayonet bend is to allow the needle to be more easily shoved along in the lumen of the vein. The arm is laid out on a cushion so as to lie flat and easy; a stout rubber tube is thrown around the middle of the upper arm and drawn tight enough to stop the flow of blood in the superficial veins, but not so tight as to impede the arterial supply, and fastened with artery forceps or a modern clip. It is very necessary that the arm should lie easy and still. The seat of operation should be wiped off with gauze soaked in alcohol. About 4 c.c. of normal salt solution are drawn into the syringe, so that by running the plunger forward the air may be expelled from the needle and from the rubber tube attached to the outlets of the two-way cock. The needle is then inserted through the skin over a vein, and run along into the vein. When the needle enters the vein a little blood flows back into the normal salt solution in the syringe. If the plunger is pressed forward, the salt solution entering the vein will distend it a little, and when it does so the tourniquet band about the arm may be removed, and the vein will collapse. Any subcutaneous vein that can be distended may be chosen, and in fleshy women Schreiber has even injected into one at the wrist. Sometimes when the vein cannot be seen it may be felt. Montgomery (Jour. Amer. Med. Assoc., Feb. 18, 1911).

The apparatus used by the writer is extremely simple. A large, heavy glass bulb-funnel, of about 500-c.c. capacity, without stopcock or stopper, is used as the receptacle. About four feet of small tubing is connected to this, with a pinch-cock and a large aspirating needle fitted to the distal end. A stoppered graduate cylinder of 50-c.c. capacity, and a pipette of 2-c.c. capacity are also required. For the preparation of the solution of the drug, only one reagent is required, a 15 per cent. solution of sodium hydroxide in distilled water. No sodium chloride or hydroxide except the C. P. should ever be employed. The sterilization of the apparatus must be carried out by boiling in distilled water. The water used in making up the solution should be freshly distilled. The writer uses a simple combination of a Jena distilling flask and a Liebig condensor for this purpose.

The patient's arm is scrubbed from shoulder to wrist and a bichloride pack applied and allowed to remain in place for at least half an hour. In case an incision is to be employed, it is well for the beginner not to make up the solution until the incision has been made and the vein laid bare; the apparatus should be boiling while the vein is being exposed.

The apparatus having been boiled for fifteen minutes in a covered dish with enough distilled water to cover the articles, the distilled water and sodium chloride solutions are put on to boil. These are conveniently contained in Erlenmeyer flasks, of about 500-c.c. capacity, with gauze stoppers. The saline solution is made up by adding 7.5 Gm. of C. P. sodium chloride to 1 liter of freshly distilled water.

About 20 or 30 c.c. of the hot sterile water is poured into the graduate, and the drug added to this. If the entire dose of 0.6 Gm. is not to be given, the deduction can most easily be made by discarding a proper proportion of the solution. The stopper is placed in the graduate and the latter shaken until a perfectly clear solution results. The writer does not use glass beads.

Two c.c. of the sodium hydroxide solution are now added from the pipette, and the graduate shaken again. A voluminous precipitate results. More alkali solution is added drop by drop, with frequent shaking, until the solution again becomes clear. The approach of the point where the clearing occurs is indicated by a darkening of the liquid. An absolutely clear solution, with not even a trace of opalescence, should be had. Keeping the solutions hot will aid in obtaining and keeping this effect.

About 350 c.c. of the hot sterile salt solution are now poured into the bulb-funnel and allowed to run rapidly through the tube and needle for a few seconds, to be sure that all air is removed from the tube. It is even well to strip the tube through the fingers, to be sure that no air-bubbles remain.

The needle is now introduced into the vein, in the direction of the blood-current. The salt solution should be flowing constantly during this procedure, to prevent the access of air to the needle-end.

When it is seen that the salt solution is flowing satisfactorily, the salvarsan solution is carefully poured into the bulb. About fifteen minutes should be allowed for the 300 c.c. to run in. When the bulb is almost emptied, 50 or 75 c.c. of saline should be added, to wash out the tube and vein. Unless the solution was almost boiling when placed in the bulb, it will be cooled down to 100° F., or so, when it reaches the needle. The temperature may be estimated closely enough by feeling the tube and needle.

When the last added saline has run through the tube for a time, the needle is withdrawn and a compress instantly placed over the opening, and held there with moderate pressure for a few minutes. If the skin has been punctured, the opening is sealed with collodion; or if an incision has been made, it is sewed up with horsehair sutures and a dry, sterile dressing applied. The patient should be in bed during the entire procedure, and it is the writer's practice to keep him there for twenty-four hours afterward. H. L. Arnold (Jour. Mich. State Med. Soc., April, 1913).

The distilled water used for making the solutions should have been redistilled and then sterilized not longer than a day before the injection. The neck of the phial containing the salvarsan may be asepticized by wiping with absolute alcohol, and the phial opened with the aid of a file previously sterilized in the flame of an alcohol lamp, but allowed partly to cool down.

Bladder disturbances after salvarsan have been shown to be due to a toxic oxidation product. Such symptoms as headaches, fever, vomiting, and diarrhea are due to dead bacteria in the distilled water. These contaminations render the patient permanently more susceptible to small doses of salvarsan and hinder further treatment. They also serve to light up other processes such as tuberculosis. Hence freshly prepared distilled water is essential. P. Ehrlich (Münch. med. Woch., Nov. 21, 1911).

Case in which the dose injected had been only 0.28 Gm., but the signs of intoxication were extremely severe, including total anuria for over twenty-four hours. The drug itself was not responsible, but rather the vehicle. During hot weather especially, a prolific microbian vegetation flourishes in the water, and although it is killed by boiling the water, yet the germs persist as albumin-containing bodies which are liable to induce serious intoxication. The only means to avoid this is to redistill afresh the water to be used for intravenous injections, and then boil it for half an hour before adding the salt solution or drug. Marschalko (Deut. med. Woch., Sept. 14, 1911).

Gratz procured samples of distilled water from not only pharmacists, but hygienic institutes. The count showed a variation of from 100,000 to 1,000,000 bacteria per cubic centimeter, the best specimens examined implying, if used as a solvent for salvarsan, an injection of at least 6,000,000. Edward Martin (Penna. Med. Jour., Nov., 1912).

The needle employed for the injection should be of fairly large caliber, and preferably of platinoiridium or tantalum. Its point should be short beveled, to diminish the risk of puncturing the vessel after the needle has once been inserted into it, but should also be very sharp, so that introduction through the skin will not require too much pressure.

Neosalvarsan, which dissolves readily in water to form a neutral solution, is prepared for injection by simply pouring into a sterile beaker 25 c.c. of freshly redistilled and sterilized water for each 0.1 or 0.15 Gm. of drug to be given, dropping the remedy in, and allowing it to dissolve, without stirring or shaking. Any turbidity remaining at the end of ten minutes means that the amount of water is insufficient. More fluid having been added, a clear solution will be formed provided the water is itself free of solid particles (Nixon). Neosalvarsan becoming rapidly oxidized on exposure to air, greater care is required to prepare the solution immediately before use than in the case of old salvarsan. A neosalvarsan solution at body temperature should *not* be used, the water being heated, if unusually cold, only sufficiently to bring it to ordinary room temperature, and *before* the neosalvarsan is dissolved in it. The solution should at no time be agitated, as this favors oxidation. The same forms of injection apparatus are used as with salvarsan. Where scrupulous care is paid to the technique, most patients suffer no discomfort whatever from the injection, though some complain of a transitory metallic taste, and occasionally there is slight headache two or three hours later. Emery observed fever after only 3 out of 600 injections of neosalvarsan.

With similar doses, neosalvarsan is better borne than old salvarsan. Intestinal disturbances and collapse are almost never observed. Drug rashes are more frequent. The activity of the preparation in man certainly equals that of old salvarsan; in animals the new preparation greatly excels old salvarsan in potency. A. Stühmer (Deut. med. Woch., Bd. xxxviii, S. 983, 1912).

The writer condemns the recommendation that ambulant patients be treated with neosalvarsan. Kall (Münch. med. Woch., Bd. lix, S. 1714, 1912).

Immediate tolerance to *neosalvarsan* is greater than to *salvarsan,* but this does not warrant use of relatively larger doses of former. Neosalvarsan is to be preferred to salvarsan where latter badly borne and in cases of **tabes, paresis, arteriosclerosis, cardiac disease,** *i.e.,* in all patients in whom too marked a reaction is to be avoided and where only small doses are indicated. Bayet (Presse méd., Dec 7, 1912).

Simple apparatus for administration of neosalvarsan described. Into a 200 c.c. Erlenmeyer flask, upon which one has scratched with a file a 100-c.c. mark, empty the ampoule of neosalvarsan. Add 100 c.c. of *freshly* distilled cold water; agitate gently until a perfect solution results, then insert a rubber stopper with two small holes, into one of which a piece of glass tubing is inserted, long enough to project above the surface of the solution when the flask is inverted, serving as an air vent. In the other opening is a short section of glass tubing, projecting externally sufficiently to attach a piece of rubber tubing three feet long, near the outer end of which is inserted a short section of glass tubing for the detection of air-bubbles. The flask may be held by someone or be fastened to a clamp or an ordinary metal towel-rack. Any good needle of sufficient lumen is plunged into the vein, the site of puncture having been sterilized with absolute alcohol, and all air-bubbles having been expelled.

While the blood and the solution are both flowing, the needle and tube are coupled. O. L. Suggett (N. Y. Med. Jour., May 17, 1913).

Since the lead salts, alkaline silicates, calcium bicarbonate, magnesia, copper, etc., that may occur in distilled water prepared in unsuitable apparatus have proven responsible for some of the untoward effects noted after injections, Ravaut simplifies matters by administering neosalvarsan in the smallest possible quantity of water that will not produce hemolysis (through hypertonicity of the neosalvarsan solution), thus rendering unnecessary special precautions in the preparation of the water.

The author has recently been injecting as much as 0.9 Gm. of neosalvarsan dissolved in only 8 or 10 c.c. of distilled water. With this procedure, the neosalvarsan itself supplies the required isotonicity with the blood instead of sodium chloride. Distilled water prepared several weeks before and kept in ampoules of the highest quality glass can be used directly without causing any systemic reaction. The solution is prepared after the constricting band has been applied to the patient's arm and the skin cleansed with alcohol. The drug is merely dropped into the water, and the solution drawn up into the glass syringe through a special glass tube containing a small wad of cotton, for purposes of filtration. The needle is then adapted to the syringe, air driven out, and the injection at once given. All rubber tubing is thus eliminated and a more strict asepsis rendered possible. The whole procedure of preparation and injection occupies only two minutes. The author has given 420 such injections without the least untoward result. Ravaut (Presse méd., April 2, 1913).

Preparation of Patient for Injection and After-treatment.—Some surgeons advise that where, as is usually the case, the volume of salvarsan solution introduced is about 250 c.c., and saline solution is employed in addition, the patient's blood-pressure should be lowered by the administration of an aperient on the evening before injection, so that the circulation will not be overloaded with fluid by the injection. The patient should have only a light breakfast on the morning of the injection, though after it ordinary meals may be taken unless fever occurs, when a milk diet should be temporarily imposed.

Rest in the recumbent position for at least two hours should be required after injection, though in patients showing no unpleasant immediate after-effects this rule has not infrequently been broken—as the event proved, with impunity. After two hours, if no symptoms have developed, the patient may be allowed to get up, but he should remain quiet for at least four hours more. Some observers advise that the patient be kept in bed for twenty-four hours. Strenuous occupation, physically or mentally, should be avoided during the entire course of the arsenical treatment (Martin).

Phlebitis and thrombosis in the injected vein should be carefully watched for; if trouble of this nature arises, the limb should be kept absolutely at rest and fomentations of lead-water and laudanum applied.

Importance of investigating the circulatory system previous to the administration of salvarsan emphasized. The blood-pressure should be estimated; if such pressure is high, 180 or over, then one should carefully observe the patient for some time before administering the drug. If he is plethoric, it will do no harm to bleed him, removing at least an equal volume of blood to the total volume of salvarsan solution—about 250 c.c.

A differential blood-count should be made before and after using salvarsan, for it will give much information should complications arise.

The urine should be observed for a couple of days after salvarsan; some patients may show a trace of albumin that is transient and rapidly disappears, while others will complain of highly colored urine for several days, which is due to urobilin. There is probably some destruction of red blood-corpuscles in almost all cases where salvarsan is administered intravenously, but very seldom does this amount to marked hemolysis. A case of marked hemolysis occurred in the author's practice, as a hematogenous jaundice following salvarsan. J. L. Boehm (Amer. Pract., Aug., 1912).

Following precautions in salvarsan administration advised: (1) Most careful technique. (2) Careful adjustment of the dose to the individual case. (3) Observation of the urinary output, as well as accurate chemical and microscopic investigation of the urine. Especially important is this in combined salvarsan and mercurial treatment. (4) Simultaneous employment of salvarsan and intensive mercurial therapy is dangerous. If the two remedies are to be given, the mercury should be carefully administered only some days *after* suspension of the salvarsan, and not given before the salvarsan. (5) Careful recording of every general reaction or rise of temperature occurring after salvarsan, and a searching inquiry into its cause. W. Wechselmann (Ueber die Pathogen. der Salvarsantodesfälle, p. 84, 1913).

Intramuscular Method.—Intramuscular injections are given either in the buttock, in the lumbar region, or in the trapezius muscle. More or less pain generally follows, and this route is therefore less acceptable from the patient's standpoint than the intravenous. In some cases, moreover, the drug becomes more or less completely encapsulated and, as a result, is only partially absorbed.

The gluteal muscles have been most used for intramuscular injections. The upper outer quadrant is the place of selection because in this region there is less danger of involving the sciatic nerve in the necrosis occurring after intramuscular injection. Another site is the extensor spinæ muscle in the lumbar region. Meltzer has advocated the use of this region because absorption is more rapid, pain is less, and no large nerve-trunks can be involved: Place the patient face downward on the bed, draw a line between the posterior superior iliac spines, select a point about half an inch above this line and one to one and one-half inches from the midline. Insert the needle (which should be about three inches long) at right angles to the long axis of the body until it has passed through the dense lumbar aponeurosis, which can be easily felt. After the needle is well in the muscle, turn it parallel to the long axis of the body and toward the ribs, and insert it nearly to the base. H. F. Swift (N. Y. State Jour. of Med., June, 1911).

The writer has made intramuscular injections in the intrascapular area and gluteal regions, but prefers the latter, as the deposits are made deeper in a large area of muscle tissue; 10 c.c. are deposited in each buttock. Injections have also been made by some in the pectoral muscles and beneath the breast. Whichever area is selected, the part should be freed from hair, thoroughly scrubbed with soap and water, scrubbed with alcohol or ether, and, if desired, painted with tincture of iodine. The area of injection should be massaged to promote absorption of the drug. Cunningham (Boston Med. and Surg. Jour., Aug., 1911).

The remedy may be given (*a*) in an alkaline solution such as that used for intravenous injection; (*b*) in a neutral suspension; (*c*) in oil.

The *alkaline solution* may be prepared in the same manner as has already been described with the exception that only enough water is added to make 20 c.c., though some surgeons use 40 c.c.

Another estimable plan is first to place the salvarsan in alcohol (ethyl) —0.5 c.c. for each 0.1 Gm. of the powder, add 20 c.c. of warm sterile water, stir with a glass rod until the drug is wholly in solution, then add, while mixing, 1 c.c. of a decinormal (4 per cent.) solution of sodium hydroxide for every 0.1 Gm. of salvarsan.

> Pain and induration from salvarsan injections are due to the sodium hydrate. The author now uses a 2 per cent. solution of sodium hydrate. He first puts the 0.6 Gm. of salvarsan in a 25-c.c. graduated cylinder, and dissolves it in 8 or 10 c.c. of hot water. The sodium hydroxide is then added in small quantities until a clear solution is obtained, care being taken not to add any sodium hydrate in excess. Hot water is then added in sufficient quantity to bring the total solution up to 20 c.c.; 10 c.c. of this solution are injected deeply into the buttocks on either side. Great care should be used to keep the injected fluid out of the adipose tissue. The sodium hydrate solution should be sterilized before each injection. B. C. Corbus (Jour. Amer. Med. Assoc., April 29, 1911).

> Intramuscular injections of acid reaction exert a more continued effect than intravenous medication, which, though more convenient and painless, permits rapid excretion of the drug. The intramuscular introduction is advisable where contraindications (heart lesions, cerebral lesions) exist. P. Ehrlich (Münch. med. Woch., Nov. 21, 1911).

> The author has given intramuscular injections of neosalvarsan in a dilution as high as 30 c.c. of water per 0.1 Gm. and noted severe pain and local swelling following. The pain seems to vary in proportion to the amount of fluid used, and as a dilution of 5 to 10 c.c. causes much less pain and local swelling, and does not increase the local or general toxic effects, the author employs that degree of concentration. The injections are made in the gluteal or lumbar regions, usually half in each side. The part is previously sterilized by painting with tincture of iodine. The author gives four injections of 0.9 Gm. at weekly intervals. General reaction phenomena have been practically *nil.*

> Just after the injection the patients experience a variable amount of pain. Injections in the intralumbar region, after the method of Meltzer, are more painful than in the gluteal regions. Ordinarily, the pain lasts several hours and gradually subsides. After about twenty-four hours there develops at the site of injection an induration, which usually is not tender to touch, or an edema, which is painless and pits upon pressure. This lasts for a few days and gradually disappears. If desired, the pain can be lessened by an injection about five minutes previously of novocaine or alypin solution. Rytina (N. Y. Med. Jour., June 29, 1912).

A *neutral suspension* of salvarsan is likely to produce less pain than an alkaline solution. It is made by adding to the salvarsan just enough sodium hydroxide to neutralize the two hydrochloric acid molecules in combination with it; the resulting free base is insoluble and can therefore only be given in the form of a suspension or emulsion. The necessity of adjusting the preparation to the neutral point renders this method more difficult to carry out than that with an alkaline solution. The salvarsan is mixed in a mortar with 1 c.c. of a saturated sodium hydroxide solution and the product dissolved in 4 c.c. of hot water. Three drops of a solution of phenolphthalein in alcohol are then dropped in. Glacial acetic acid is next added in successive drops until the preparation changes in color from red to yellow, and, finally, one or more drops of the sodium hydroxide solution added until a pink color again begins to appear.

A simpler method of preparing the neutral emulsion is that of Citron, who adds to the salvarsan 1 c.c. of absolute alcohol and 5 c.c. of hot water, and stirs until complete solution has been effected. Finally, 40 drops of a 10 per cent. solution of potassium bicarbonate are mixed in, and the preparation gently agitated with a glass rod until a very fine suspension or emulsion results.

Oily preparations of salvarsan are still advised by some, though it seems to be the opinion of many that the therapeutic effects are less marked than with the alkaline solution. Some claim it as an advantage, on the other hand, that the subsequent pain is relatively slight. Various menstrua have been recommended. Kromayer rubs up the drug with paraffin oil (liquid petrolatum) so that every 1 c.c. will contain 0.1 Gm. of the remedy, and administers fractional doses of 0.1 to 0.2 on alternate days; he asserts that if the injections be made slowly, pain and swelling will rarely, if ever, follow. Burke gives the drug in an olive-oil mixture containing 10 per cent of anhydrous wool-fat; enough of the menstruum is rubbed up with the salvarsan to make a mixture that will pass through the needle, and 4 or 5 drops of the U. S. P. 5 per cent. sodium hydroxide solution then added, breaking down the lumps so that the emulsion becomes a soft mass. Lydston suspends the salvarsan in from 3 to 6 c.c. of 10 per cent. iodized oil of sesame.

Hazen employs an oil of the following composition:—

℞ *Camphoræ,*
Guaiacolis ....āā ʒss (2 Gm.).
Petrolati liquidi, q. s. ad ℥j (30 c.c.).—M.

Just enough of the oil is used to make a fine, smooth emulsion—usually about 5 c.c.—the salvarsan being first placed in the mortar, previously boiled and allowed to dry, and the oil then added drop by drop, the mixture being meanwhile carefully ground.

> The technique of an oily injection is simple. All that is needed in addition to the oil and salvarsan is a suitable syringe and a small mortar and pestle. A 5-c.c. syringe may be used, but one in which the end of the plunger is cut off square, and not round, as in the latter case some of the emulsion may work up between the plunger and barrel of the syringe and jam. The portal of exit of the syringe should be large, and a needle of from 17 to 20 gauge used. About 0.5 c.c. of air is injected along the needle so as to prevent the oil from escaping into the subcutaneous tissues. The injections may be made into either the gluteal or lumbar muscles. A small injection of 0.3 Gm. gives even less trouble than a full injection; so it is wise to give two half-doses at one sitting rather than a full dose. The results have been about the same as with the other types of intramuscular injection; most of the secondary skin manifestations and all the mucous patches, condylomata, and throat ulcerations cleared up speedily, while some of the tertiary lesions did very well and some were uninfluenced. Hazen (Wash. Med. Annals, Sept., 1912).

In executing any of the intramuscular or subcutaneous procedures, due aseptic precautions should be taken, the syringe and needle being boiled, sterile receptacles, including the mortar and pestle, used, and the skin disinfected. Where an oily preparation is to be used, a needle of wide caliber — 17 to 20 gauge — must be employed, and both the syringe-body and the needle must be absolutely dry. Hazen advises that after being boiled they be cleaned with alcohol and ether, or, better, that they be sterilized by dry heat. The preparation to be injected should always be freshly made, as salvarsan becomes partly oxidized on standing, with the formation of more toxic derivatives.

Great care is to be taken, in injecting an oily preparation or suspension, that none of the fluid gets into a vein. The simplest plan is, after inserting the needle, to wait a short period before connecting the syringe-barrel with it, to see if any blood exudes. Burke recommends that one syringe be half-filled with the oily menstruum unmixed with salvarsan, and the piston be drawn upon, making suction on the oil. If a vessel has been punctured the oil will be blood-stained, in which case the needle should be taken out; if it is not, the first syringe is detached and replaced by another containing the salvarsan mixture. After the injection is finished the salvarsan syringe may be replaced by the pure-oil syringe and a little oil injected, to avoid leaving a trail of salvarsan along the needle-track. The needle should be withdrawn quickly, pressure being made at the same time over the site of injection.

Neosalvarsan may be given intramuscularly either in sterile water, saline solution, or glycerin. Theoretically, it should be superior to salvarsan owing to the fact that a neutral solution can be administered. Nevertheless neosalvarsan injections have proven decidedly irritating, causing transitory pain, inflammatory swelling and edema at the point of introduction. As in the case of salvarsan, therefore, intravenous administration of neosalvarsan is preferred by nearly all who have used the two methods. Hazen himself prefers the intravenous route to the oily injections. For intramuscular injection a solution in 5 to 10 c.c. of sterile water is most employed. The use of 0.4 or 0.5 per cent. saline solution is disadvantageous in that turbidity results, and according to Schreiber the preparation becomes more toxic. Absorption of neosalvarsan is more rapid than with salvarsan, and less local induration is caused.

> The effects of neosalvarsan are at least as striking as those of salvarsan. The neutral reaction of the solution in water obviates the use of sodium hydrate, thus avoiding the possibility of thrombosis. Leakage of neosalvarsan solution into the tissues seems to be absorbed much more quickly than salvarsan. The author advises for intramuscular injection a suspension of neosalvarsan in glycerin. The powder is mixed in a mortar with 3 to 4 c.c. of glycerin, to which are added a few drops of a 1 per cent. beta-eucaine or alypin solution in distilled water. The suspension is now converted into an almost clear solution. The buttocks are painted with iodine and four spots are located into which 1 c.c. of the solution is injected. Most patients feel practically no pain; some feel pain on sitting or standing for a day or two. The induration caused by the injection is very slight. Wolbarst (Med. Rec., July 27, 1912).

Intramuscular injections of neosalvarsan in oily suspension are as safe for general use as similar injections of calomel or metallic mercury. To minimize pain the amount to be injected—generally 0.3 Gm.—is administered in two places. The first two injections are given in the lumbar region, just above the iliac crest, the second one and a half or two centimeters above the first. The patient, lying prone with the arms extended, is told to contract the dorsolumbar muscles, when, after cleansing of the skin with alcohol, the needle is inserted perpendicularly at the most salient point of the muscles, to about one-half the depth (thickness) of the latter. A small wad of cotton is introduced into the shank of the needle to detect any escape of blood from vascular injury, and if none appears, the sterile syringe barrel, into which the oily suspension has just been poured from its ampoule, is adapted to the needle and the injection made. Upon quickly withdrawing the needle, pressure is made over the puncture and a small piece of diachylon plaster applied. Five or six injections can be given in each dorsolumbar region; when the buttock is used, its upper and outer segment should be selected. The amount of oil injected at each sitting is only 1 c.c. (16 minims), one-half in each injection. The pain is scarcely ever sufficient to deter patients from returning for regular weekly treatment. From four to six injections of 0.3 Gm. are generally sufficient. Mercury is then given, followed by two series of three or four neosalvarsan injections in the first year after the beginning of treatment. Additional series should be given in the succeeding three years. F. Balzer (Presse méd., April 2, 1913).

Fifty-eight oily injections given to 44 individuals. Fifty-two were of salvarsan and six of neosalvarsan. In general the effects on the lesions and on the Wassermann reaction were excellent. Twenty of the injections were practically painless, and only twelve caused pain that was at all severe. Two, however, developed slight abscesses of no particular import; one developed peripheral phlebitis about two weeks later; and the most serious accident was pulmonary embolism, the patient fortunately recovering in about two weeks.

In 6 instances abscess at the site of injection developed in from three to twenty-four months after treatment. In 1 of these patients both buttocks broke down about three months after injection, although the injection was unilateral. In 1 case, exactly two years after the administration of salvarsan, an abscess pointed in the buttocks. It was opened, and about 6 ounces of sterile pus and considerable tissue *débris* were evacuated. In another case five small injections were given at biweekly intervals without any especial trouble, but about three months after the last both buttocks became red, swollen, and painful, with distinct fluctuation. One other patient has had permanent nodules left in his buttocks, and complains bitterly of pains radiating down both sciatic nerves.

The material injected is evidently toxic to tissue at the site of injection, and this dead tissue, if not absorbed, may act as a foreign body. In the abscesses opened no trace of salvarsan could be found.

After the use of neosalvarsan in water one must be prepared for severe pain. The author has seen one patient rendered absolutely helpless for three weeks. Nor does the administration of neosalvarsan in glycerin work any better. Oily injections of neosalvarsan are more painful than when salvarsan is used. Out of six injections 3 patients experienced great discomfort. The intravenous method should be the only one employed. H. H. Hazen (Jour. Amer. Med. Assoc., May 24, 1913).

Subcutaneous Method.—The pain and local necrosis caused by subcutaneous injections of salvarsan are so marked that this procedure has been abandoned. Neosalvarsan was found by McIntosh, Fildes, and Parker to be practically painless when injected only in the dose of 0.1 Gm., but necrosis of the subcutaneous tissues nonetheless resulted, and induration was but slightly diminished after three months.

Rectal Method.—This is, of course, a somewhat imperfect and probably uncertain mode of administration which should be employed only under exceptional conditions. The most pronounced results are not to be expected from it.

Weill, Morel, and Mouriquand have advised its adoption in children, in whom intravenous injections are not easily given, *e.g.*, in cases of severe chorea, inherited syphilis, anemia, etc. Most of the observers who have employed this route for adults have later abandoned it.

> The author incorporates 0.1 Gm. of salvarsan into an ordinary suppository, which he introduces into the rectum. The patients are not allowed to go to stool for ten or fifteen hours, and it is then found that the feces do not contain any visible traces of salvarsan. It is possible to see clinical improvement three to four days after the introduction. Bagrow (Berl. klin. Woch., Jan. 15, 1912).
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> In some children from 10 to 13 years of age successive doses of 0.10, 0.20, and 0.40 Gm. of salvarsan were given by rectum. The drug was prepared as though for intravenous injection, mixed with about 100 c.c. of 0.5 per cent. salt solution and 5 or 10 drops of laudanum, and slowly administered through a tube introduced as deeply as possible into the rectum. Care was taken to have the fluid retained at least four hours. In each case treated pronounced improvement was noted. Barring emergency cases, rectal administration is the method of choice for giving salvarsan to children, since along with sufficient activity of the drug there is an entire absence of unpleasant reactions, local or general. Weill, Morel, and Mouriquand (Lyon méd., July 7, 1912).

External Application. — Various kinds of ulcers, including those of syphilis, chancroids, Vincent's angina, may be advantageously treated externally with a mixture of salvarsan or neosalvarsan and some bland substance such as bismuth subnitrate.

> Salvarsan used locally on non-syphilitic abscesses of the gums, tongue, and lips. The author found microscopically a great number of spirochetes, which disappeared after three days of treatment, resulting in absolute cure. The method consisted in the use of physiological salt solution at body heat, followed by an application with a brush of a 10 per cent. watery salvarsan solution, repeated three times a day. Zilz (Münch. med. Woch., Jan. 2, 1912).
>
> Neosalvarsan successfully injected into the lumbar sac of the cord. In no case was there any reaction. The general interest of further experiments along these lines consists in determining the utility of this method of local treatment in meningitis luetica, meningomyelitis, and tabes. In all probability increasing doses will be found necessary. Wechselbaum (Deut. med. Woch., Aug. 1, 1912).
>
> In a case of **parenchymatous keratitis** energetic mercurial treatment had not prevented the extension of the process to the second eye. The author applied a little neosalvarsan in powder to one eye and instilled a few drops of a 2 per cent. solution into the second eye. The extension of the process was at once checked in both eyes and the cornea soon commenced to clear up. It may be of advantage to apply the neosalvarsan suspended in an oily solution of atropine, as decomposition of the drug is prevented in this way. L.

Rosenmeyer (Münch. med. Woch., Nov. 5, 1912).

Observations indicating how the untoward effects of salvarsan, when locally applied, can be avoided: Mix the compound with liquid petrolatum in the proportion of 1 part of salvarsan to 10 of petrolatum. The best results were obtained by using neosalvarsan in the same manner. It seemed to produce less irritation than salvarsan and not to coagulate albumins. It penetrates more energetically the pathological tissues. Cicatrization of **soft chancre** was found to occur very rapidly at first, the healing process then becoming less active. Nevertheless, even large, soft phagedenic processes yielded in from six to twelve days. Melun (Thèse de Paris, 1913; N. Y. Med. Jour., April 5, 1913).

CONTRAINDICATIONS. — Salvarsan is usually contraindicated in the presence of severe non-syphilitic visceral diseases, especially those affecting the heart, kidneys, and liver. In cases of aneurism, the injection of the remedy is considered hazardous, though certain French clinicians have used salvarsan in this condition with asserted good results. Well-compensated valvular lesions in young subjects do not contraindicate it. In syphilitic myocarditis there is some risk, but good results may be obtained with small doses. Arteriosclerosis is a relative contraindication, more particularly where the intracranial vessels are involved, as the rise of intracranial pressure and local reaction produced may lead to hemorrhage.

Syphilitic aortitis complicated with heart-muscle degeneration—especially the triad, syphilitic aortitis, sclerosis of the coronary arteries and myocarditis—forms an absolute contraindication against the use of salvarsan. **Angina pectoris** without complication of heart muscle is most favorably influenced by salvarsan. K. Martius (Münch. med. Woch., May 16, 1911).

Salvarsan is chiefly indicated where changes in the heart muscle are still reparable and slight. In the tertiary stage, bradycardia would be an absolute contraindication, while with tachycardia a cicatrix may not yet have formed, so that the chief lesion is still a gummatous infiltration. It must be remembered, however, that the rapid absorption of gummatous tissue may leave a weak spot in the walls of the heart which might rupture. Salvarsan is absolutely contraindicated in acute rheumatic endocarditis, severe non-specific myocarditis, and severe cardiac complications of kyphoscoliosis, Basedow's disease, goiter, emphysema, lung affections, non-specific arteriosclerosis, and nephritis. It is indicated, however, in the early stages of lues, where the chief symptoms are arrhythmias, tachycardia, palpitations, dyspnea, anginal symptoms, accidental murmurs without endocarditis, aortic insufficiency, provided there is no pronounced dilatation or functional insufficiency. In tabes or general paresis with heart or arterial disease, the drug should not be employed. M. Breitman (Berl. klin. Woch., Sept. 25, 1911).

Albuminuria, if not marked, is not held to be a contraindication, as it may be due to the syphilitic infection, and be actually benefited by the remedy. Caution as to dosage is, however, necessary in these cases. The presence of casts in the urine is a contraindicating circumstance. Diabetes is likewise a contraindication, though sometimes glycosuria in syphilis is the result of syphilitic catarrh of the pancreas. Nixon, referring to the fact that the urine should always be examined before giving an injection, advises that one make sure in particular that the quantity secreted is normal, the specific gravity within healthy limits, and, above all, that the excretion of urea is sufficient.

Where the liver is in a pathological state, salvarsan will tend to accumulate therein more than if it is normal, and is likely to cause additional destructive changes in the cells, whence acute yellow atrophy may develop. Catarrhal jaundice in early secondary syphilis is not a contraindication, but later, when jaundice is due to gummatous formations involving the parenchyma, the drug should not be given (McDonagh). In debilitated alcoholics, or those suffering from cirrhosis, salvarsan should not be employed.

In syphilitic disease of the central nervous system, particularly where there are signs of cerebral or spinal meningitis, psychic disturbances, optic neuritis, or epilepsy, special caution is necessary, and the dose given should not exceed one-half the usual amount. In cases of bulbar paralysis the drug had best be entirely withheld. It is to be borne in mind that with large doses the reaction is much more marked than with small. Especially at the beginning should the dosage be extremely guarded. Cases of general paralysis in which the diagnosis is obvious, late cases of tabes with negative Wassermann reaction, acute cases of cerebrospinal syphilis, and nervous disorders in congenital syphilis contraindicate salvarsan (McDonagh).

> Following contraindications to salvarsan enumerated: (1) non-luetic diseases of the optic nerve and retina; (2) neuroses and organic diseases of the heart and blood-vessels; (3) severe diseases of the lungs, excepting tuberculosis if there is no hemoptysis; (4) severe non-luetic nephritis and diabetes; (5) severe visceral lues, ulcers of the stomach; (6) advanced degeneration of the nervous system and alcoholism; (7) severe congenital lues of the newborn; (8) febrile diseases of various kinds; (9) menstruation; (10) senile degeneration, non-luetic marasmus and cachexia. Stülp (Klin. Monatschr. f. Augenheilk., March, 1911).

> Special precautions and a preliminary course of mercury are indicated in all syphilitic cases giving symptoms of cerebrospinal involvement as suggested by alteration in temperament, mentality, and business capacity, headache and backache, insomnia, tinnitus, vertigo, and muscular asthenia. In cases characterized by advanced cardiac insufficiency, hepatic cirrhosis, renal degeneration, or intercurrent acute infection of other than spirochetal origin, the drug should be used in minimum quantities if at all. Edward Martin (Penna. Med. Jour., Nov., 1912).

> In applying salvarsan therapy great caution is to be used in cases where the slightest defect in hearing is already present. Rimini (Deut. med. Woch., Jan. 9, 1913).

Cases of pulmonary tuberculosis in the third stage should not be given salvarsan, as hemoptysis might result. Non-syphilitic epilepsy contraindicates salvarsan. Advanced age is also a contraindication.

> Salvarsan should be avoided in severe affections of the brain or heart, in putrid bronchitis, in severe diabetes, and in all conditions of decrepitude. Hirschfelder (Jour. Amer. Med. Assoc., Nov. 18, 1911).

PHYSIOLOGICAL ACTION.—Our information on this subject is in a somewhat fragmentary state, the researches conducted having dealt chiefly with the lethal dose, the mode of elimination, the question of storage of salvarsan in various organs, and its effects on the tissues from the histological standpoint.

Toxicity.—Kochmann found that intravenous injections of salvarsan in rabbits caused death only when the amount of elemental arsenic contained in the salvarsan introduced was 0.034 Gm., as compared with 0.00456 to 0.0053 Gm. of sodium arsenate. The toxicity of salvarsan is thus far lower than that of inorganic arsenicals. Kolmer and Schamberg found that salvarsan could be given by mouth in pills, capsules, or solution, in mammals, in the dose of 0.02 to 0.03 Gm. per kilogram of body weight without causing toxic symptoms. A dog was thus given 0.57 Gm. in the course of twenty-nine days without any disturbance resulting.

> Salvarsan is a comparatively inactive drug when applied directly to nerve and muscle tissue of the frog. In bathing experiments, in which the concentration of the salvarsan in the various solutions was much higher than that in which it reaches the peripheral tissues in the human subject, the loss of irritability occurred only after a long period of exposure to the drug. Joseph (Jour. of Exper. Med., June 1, 1911).

Storage and Elimination.—Salvarsan remains in the circulation for some time after intravenous injection, as was shown by Abelin in 1912 in a series of 8 human cases. Possessing apparently a selective affinity for certain tissues of the body, it—or some derivative—tends to collect in the liver and the kidneys. According to French investigators about three times as much arsenic is temporarily stored in the liver as in the kidneys. The question as to whether there is an affinity of the central nervous tissues for salvarsan, such that the drug might sometimes be directly responsible for untoward nervous phenomena in syphilis, has been fairly conclusively settled in the negative. Morel and Hugounenq, while they noted an evident "neurotropic" tendency in the case of arsenic acid, failed to find it with salvarsan. Beck, from experiments on mice, reached the conclusion that salvarsan exerts no toxic effect upon the nerves of the head, including the auditory nerve.

> Several cadavers of individuals dying of intercurrent affections from two weeks to several months after injection of salvarsan examined. In one cadaver two weeks after injection 6.5 mg. of arsenic was found in the liver; 3.1 mg. in the kidneys, and 1.8 mg. in the spleen. Bornstein (Deut. med. Woch., Jan. 19, 1911).

> Intravenous injections of salvarsan in the rabbit deposit arsenic in the organs, especially the liver. Ritter (Deut. med. Woch., Jan. 25, 1912).

> Cerebrospinal fluid examined in 17 cases of syphilis to each of which 0.6 Gm. of salvarsan was given intravenously. The fluid was withdrawn at intervals of from fifteen minutes to forty hours after the injections. Doses up to 0.6 Gm., or perhaps more, do not ordinarily result in the presence of any arsenic in the cerebrospinal fluid. Arsenic is present in the fluid practically only when the dose is so large or so frequently repeated as to cause a meningoencephalitis, which is sometimes of a fatal character. The assumption that the introduction of salvarsan into the blood-stream causes it to reach all parts of the body was not substantiated. Camp (Jour. Nerv. and Mental Dis., Dec., 1912).

> Experimental study in which the amounts of arsenic found in the brain, including cerebellum, medulla, and cranial nerve-roots, after salvarsan, were no greater than in untreated animals, though in one instance the combined medulla and spinal cord

> showed a slight excess. Almost always large amounts—up to 0.14 per cent.—were found in the liver. The kidneys contained only a relatively small amount, sometimes only a trace. The bile and heart, in the one instance in which they were examined, showed 0.2 per cent. and 0.083 per cent., respectively. These results do not agree with those of Mouneyrat, who concluded that salvarsan was distinctly neurotropic. A. Morel and G. Mouriquand (Lyon méd., Feb. 9, 1913).

When injected into the muscles, salvarsan is only slowly and imperfectly *absorbed.* Neosalvarsan, according to Swift, is taken up much more rapidly, between 75 and 85 per cent. of the arsenic being absorbed in the first week—the remainder, however, quite slowly, so that at the end of six weeks 5 per cent. of the arsenic is still present in the injected muscle. Ullmann and Haudek already in 1911 emphasized, on the basis of X-ray experiments, the advantages, where salvarsan was to be administered hypodermically, of dividing the dose into several small ones given at different points, as only a small proportion of large doses was absorbed and the remainder merely injured the tissues at the point of injection.

> The rate of absorption is most constant after the intramuscular injection of the neutral suspensions, a little more irregular after the injection of the alkaline solution, and most irregular after the injection of the acid suspensions. This is what might be expected if the rate of absorption is dependent upon the degree of injury produced by the injection, since neutral solutions inflict the least injury. During the first week after intramuscular injections of neosalvarsan as much arsenic is absorbed as after six weeks of salvarsan. Swift (Jour. Exper. Med., vol. xvii, p. 83, 1913).

The *excretion* of salvarsan takes place chiefly through the kidneys, and to a less extent by the intestines, skin, and lungs. Its rapidity is subject to marked variations according to the mode of introduction. Escallon, studying the urinary elimination of salvarsan by means of Abelin's color reaction, found that the curve of excretion showed two maximal points, the first in the four or five hours just after the injection and the second twenty to twenty-eight hours or sometimes forty-eight hours after it. In the interval between the two summits of the curve, the excretion was markedly lessened and sometimes even at a standstill. The duration of the elimination and the total amount excreted were found to increase with each successive injection. According to Abelin the excretion of salvarsan begins in from five to fifteen minutes after an intravenous injection. Fischer and Hoppe found only traces of arsenic in the urine three days after the introduction of salvarsan by this route. The arsenic excretion may thus be considered finished on the fourth day after intravenous use. That this is not invariably the case, however, was shown by Bornstein, who found arsenic in the urine three weeks after intravenous injection.

> With the Marsh test, the author obtained a marked reaction for arsenic in the urine twelve and fourteen days after a single intravenous injection of 0.5 Gm. With intramuscular injections of the alkaline solution, arsenic could be detected after more than four weeks. H. F. Swift (N. Y. State Jour. of Med., June, 1911).

> The author found considerable fluctuation of the arsenic content of the urine after salvarsan. The length of time during which arsenic may be found in the urine varies with the method of administration: In intravenous injection, from nine to sixteen days; in intramuscular, from twenty-five days to six months. In a nursing woman who received salvarsan, arsenic was found in the milk. Merkurjeff (Roussky Vratch, June 9, 1912).
>
> In 1 patient with albuminuria, elimination began only twenty-nine hours after injection and continued sixty-nine hours; in this patient a roseola developed a few hours after the injection, followed by diarrhea, vomiting, and headache. Abelin's reaction is valuable to ascertain before repeating salvarsan that the preceding dose has been completely eliminated. It is performed by adding to 7 or 8 c.c. of urine, acidulated with a few drops of decinormal hydrochloric acid, 3 or 4 drops of 10 per cent. sodium nitrate solution, followed by a few drops of a 10 per cent. alkaline solution of resorcinol and a drop or two of sodium hydrate solution. If the urine contains salvarsan in notable amount, a red color develops; if only in traces, a pink color. The reagents used should previously have been cooled in ice-water. This test lends itself readily to colorimetric determinations which are sufficiently accurate for clinical purposes. Escalon (Lyon méd., Sept. 8, 1912).

Fischer and Hoppe showed that after intramuscular administration of salvarsan, somewhat less than one-half the whole amount can be recovered from the urine, and that the elimination is not complete for twelve days. In one fatal case arsenic was found in the gluteal muscles thirty-six days after the injection. It seems unquestionable that the local necrotic changes and partial encapsulation occurring after these injections exert a marked retarding effect upon the absorption of salvarsan, and, in addition, that the rate of absorption and consequently the intensity of therapeutic action as well as the rapidity of elimination are subject to pronounced variations in different cases—another disadvantage of the hypodermic routes of administration as compared to the more direct intravenous method.

> Arsenic can be found in some cases six and nine months after an intramuscular injection and as much as three months after an intravenous injection. Heuser (Med. Klinik, April 9, 1911).
>
> Experiments made with gastric contents, feces, bile, and urine which demonstrated that within twenty-four hours after *ingestion* of salvarsan, arsenic may be found in both bile and urine. Probably only a portion is absorbed, and this is quickly eliminated. J. A. Kolmer and J. F. Schamberg (Jour. Exper. Med., vol. xv, p. 498, 1912).

Effects on Circulation, Blood, and Urinary Apparatus.—Salvarsan does not appear directly to depress the normal heart and blood-vessels to any marked extent. A temporary fall in blood-pressure and slowing of the heart rate has, however, been reported to follow its intravenous injection in some instances. Concerning its effects on the blood-cells the results of investigation have been contradictory. Normal kidneys, so far as is known, do not suffer from the presence of pure salvarsan, though where the drug has been allowed to undergo oxidation before use a tendency toward diminished renal activity or even anuria may be manifest.

> Three cases of brain disease were given 0.5 to 0.6 Gm. of salvarsan and

the effects of the latter studied. The blood-pressure was but little influenced—twice slightly raised and once slightly lowered. Immediately after the injection the urinary flow was increased. The nitrogenous constituents of the urine were somewhat diminished, though there was an increase of uric acid and purin bases. Fever followed the injection in each case and lasted five or six days, during which there was oliguria and retention of nitrogens and sodium chloride. In all 3 cases urobilin was found to a considerable extent in the urine, and this condition lasted as long as the fever. Arsenic was found sooner and remained longer in the urine than in the feces. It could still be detected in the urine three weeks after the injection. A temporary increase in the number of both red and white blood-cells took place after the injection, though no abnormal cellular forms were found. Rzentkowski (Gazeta Lekarska, July 30, 1911).

Intravenous infusion of 0.5 per cent. alkaline salvarsan causes no marked apparent effect on the heart in dogs, but its factors of safety may be so reduced in some instances that a slight extra strain produces fibrillation and death. The animals stood the infusion of salvarsan in 0.2 per cent. or 0.5 per cent. alkaline solution very well, even with the enormous doses infused (20 to 40 mg. per kilo of body weight). No marked changes of either heart volume, blood-pressure, or heart rate were recorded. Auer (Jour. of Exper. Med., Sept., 1911).

Blood of 21 patients studied both before and after the intravenous administration of salvarsan. There was no change in the erythrocytes beyond physiological limits after the injection, except where there was a more or less severe systemic reaction, when a distinct fall in their number occurred. There was a definite relationship between the systemic reaction and the use of stale distilled water. Salvarsan itself seemed to play no part in reducing the count. G. M. Mackee (Jour. of Cutan. Dis., April, 1912).

Blood examinations made in 7 cases treated with salvarsan. The majority showed a slight increase in the number of reds and an average increase of about 5 per cent. of hemoglobin in the interval of a week that elapsed between the two estimations. The number of whites varied somewhat with the condition and was naturally higher in cases in which ulceration was present with consequent absorption, but neither a constant increase nor decrease in the number of leucocytes was observed after the injection. The differential counts showed nothing of interest. Flint and Cunningham (Yale Med. Jour., May, 1912).

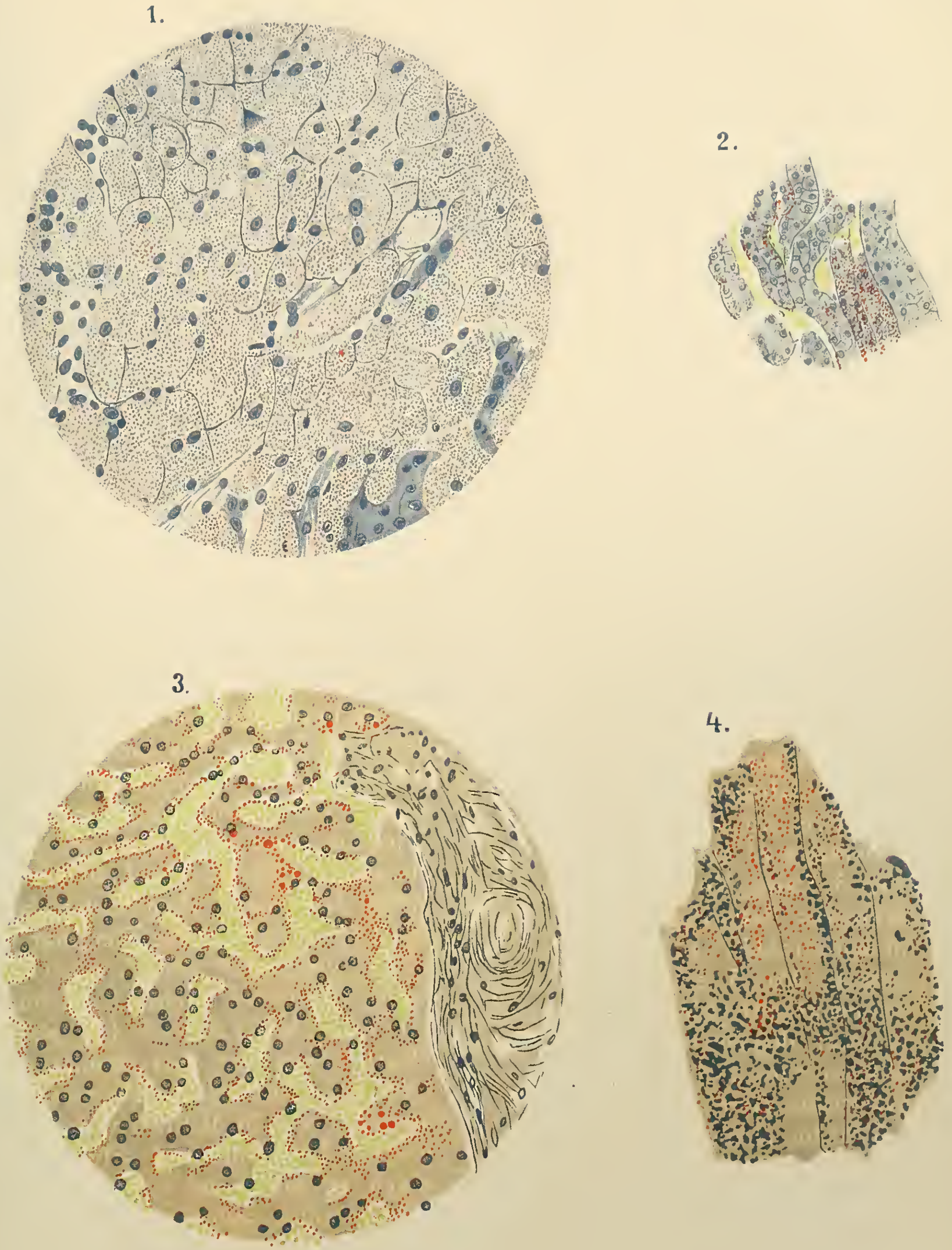
Histological Alterations Produced in the Viscera.—The incidence of these alterations appears to depend, at least in so far as experimental work would indicate, upon two factors: (1) the dose given, and (2) individual susceptibility or idiosyncrasy. The work of Kolmer and Schamberg in animals, to which the doses administered—by mouth—were, in their opinion, about equivalent to those given intravenously to man, seemed to show that in ordinary amounts given to healthy animals, salvarsan does not produce appreciable degenerative changes in the principal organs within a period of four days. With larger though still sublethal doses, however, fatty changes were found by Chirokogorov to have occurred in a certain proportion of the animals experimented upon. The doses used by this author were 0.05 to 0.2 Gm., given subcutaneously or intramuscularly. In 2 of the 4 rabbit experiments of which he gives protocols, the heart showed a mild degree of fatty change and the liver fat globules decidedly in excess of those normally present in the cells; one of these rabbits also showed abnormal fatty changes in the kidneys. Two dogs weighing about 17 and 20 kilograms and given, respectively, 0.5 and 0.6 Gm. of salvarsan, when sacrificed showed no fatty changes in any of the organs. Pronounced changes in the liver, however, were found in mice given lethal doses. The final conclusion reached by Chirokogorov is that salvarsan undoubtedly does sometimes produce fatty changes, but that the tendency to this varies in different species and also to a wide extent in different individuals of the same species. [The degenerative changes found by Chirokogorov in one of the rabbits are shown in the annexed plate: Fig. 1. Zeiss, 1/12 oil immersion, No. 2 eyepiece: Fatty degeneration (red granulations) in heart muscle of a rabbit weighing 800 Gm. and given subcutaneously 0.05 Gm. of salvarsan. Fig. 2. Zeiss, E objective, No. 4 eyepiece: Fatty degeneration of kidney in same rabbit. Fig. 3. Leitz, No. 3 objective, No. 3 eyepiece: Fatty degeneration of liver in same rabbit. Fig. 4. Zeiss, E objective, No. 3 eyepiece: Muscular lesions at seat of injection, consisting of fatty degeneration, accumulation of leucocytes, and partial hyaline degeneration of the muscles.]

That the variations observed among different individual animals by Chirokogorov hold good likewise in man is suggested by the histological changes seen in certain of the salvarsan fatalities in the human subject. Thus, among 18 cases of death following salvarsan collected by Martius, a few only showed fatty degeneration of the heart, liver, and kidneys. Hofmann reported the production of subacute yellow atrophy of the liver in a boy 5 years old by two salvarsan injections. Fischer witnessed a case of death from acute encephalitis in which changes were found in the heart muscle, liver, and brain-cells.

UNTOWARD EFFECTS AND POISONING.—Toxic symptoms following salvarsan injections may arise either independently of the drug, *i.e.*, from an improper manner of administration, or because of some direct or indirect effect of the drug itself.

The use in the preparation of salvarsan for intravenous injection of water that has not been redistilled a few hours before very frequently leads to the appearance of headache, fever, rigors, and vomiting, owing to the effects of the toxins from saprophytic bacteria or fungi that have grown in the distilled water in the intervals. Before this fact had been discovered by Wechselmann the untoward effects following intravenous injection were attributed largely to the salvarsan itself. That old distilled water is actually their cause, however, is proven by the fact that the same symptoms occur when the water is injected alone. Experimental work by Yakimoff has shown clearly, moreover, that simultaneous injection of bacterial endotoxins, such as may occur in distilled water, lowers the lethal dose of salvarsan as much as three and one-half times. Where saline solution is made from distilled water, experience has shown that it should preferably be boiled again after the salt has been dissolved.

Report on the use of salvarsan in a man, aged 33, suffering from secondary syphilis, with resulting diarrhea followed by constipation,



Degenerative Changes Occurring in a Rabbit After the Administration of a Non-lethal Dose of Salvarsan. *(Chirokogorov.)*

Archives des Sciences Biologiques, St. Petersburg.

syncope, retention of urine with albuminuria, meteorism, and loss of reflexes. The patient was the only one thus affected out of 72 treated. The author in treating this case used the remnants of two tubes, one having been open for fourteen days and the other for three days. Eitner (Münch. med. Woch., Bd. lvii, Nu. 45, 1910).

Through the influence of salvarsan, reactions from bacterial toxins will appear after the injection of the drug, if such toxins exist in the blood in large-enough quantity to produce such reactions. Such bacteria may be introduced through the distilled water if this is not entirely fresh, or exist in the body through infection. Almkvist (Deut. med. Woch., Jan. 4, 1912).

Ehrlich concludes that in nearly every instance the main factor in the mortality has been an error in technique and that the majority of cases would have been saved if pure water was used. Yakimoff showed by animal experiments that the toxicity of salvarsan is enhanced by the introduction of dead bacteria, which cause the body-cells to anchor the salvarsan more firmly. J. A. Fordyce (Jour. Amer. Med. Assoc., Oct. 5, 1912).

It has been clearly established that most of the untoward results from salvarsan and neosalvarsan have been the result of improper or careless administration. Men of large experience have made thousands of administrations with few or no unfavorable results; while those who report complications have made relatively few administrations. Malaise, headache, nausea, vomiting, chill and febrile disturbance attending the administration, are expressions of faulty technique. Some have stated that the attending reaction is in direct ratio with the amount of syphilis present. The writer feels positive that, under proper conditions, intravenous administration of neosalvarsan will produce little or no disturbance in highly active and severe infections. M. L. Heidingsfeld (Lancet-Clinic, March 22, 1913).

Excluding the phenomena already referred to, there may occur in a minority of cases various symptoms due to unusual susceptibility of the patient to arsenic or to toxins set free owing to the action of salvarsan on the spirochetes or the patient's tissues. Some of these symptoms are identical with those due to old distilled water, viz., headache, malaise, vomiting, and prostration. But there may also be noted pain in the abdomen, diarrhea, jaundice, somnolence, angina, skin eruptions, and in the unusual serious cases, coma due to hemorrhagic encephalitis or ininvolvement of the kidneys and liver. (Hemorrhagic encephalitis has likewise been attributed to old distilled water). Where the drug is given in suitable dosage and with correct technique to individuals that are not unusually susceptible to arsenic, the only symptoms to be expected are slight anorexia and a sensation of physical depression not exceeding a day in duration (Martin).

Retention of urine for from half a day to over nine days, abolition of the knee-jerk and of other common reflexes, and extreme rectal tenesmus with obstinate constipation, occurred in more or less pronounced form in 3 patients after moderate doses of salvarsan. K. Bohac and P. Sobotka (Wiener klin. Woch., July 28, 1910).

Case of collapse five hours after an intravenous injection of 0.45 Gm. of salvarsan in alkaline solution. The danger was promptly recognized and stimulants applied, soon restoring the patient, a robust young woman in the second stage of syphilis. In another case the collapse occurred in the night after subcutaneous injection, and nothing was known of it in time.

The heart was not quite normal in either of these cases, but the collapse was the result of arsenic intoxication. Great attention must be paid to the heart both before and after the treatment, and tobacco and alcohol must be avoided for a time. One young man, attnding a party eight days after injection of 0.6 Gm., drank a great deal and smoked cigarettes, neither of which had ever previously affected him. The next day acute heart weakness developed, with which he had to contend for weeks. Myocarditis and heart defects contraindicate the use of salvarsan, as also affections of the central nervous system localized in vital centers. Spiethoff (Münch. med. Woch., Jan. 24, 1911).

The author injected 0.2 Gm. of salvarsan into the left gluteal muscle of a 9-year-old girl with parenchymatous keratitis; there was slight spastic paresis in the right leg and the Wassermann reaction was positive, although the parents denied syphilis. Eighty-one hours after the injection the child was found unconscious in collapse, and epileptiform seizures developed, with pulse 160, extreme cyanosis and foam at the mouth. The child gradually recovered in four or five days. Slight paresis suggesting a possibility of meningitis in the past should contraindicate salvarsan unless the patient can be kept under constant clinical supervision. Gilbert (Münch. med. Woch., Feb. 14, 1911).

A patient developed intercostal herpes zoster thirteen days after an intramuscular injection of salvarsan. The symptoms were not quite so pronounced as in ordinary infectious herpes. Another patient had an itching erythema over all the covered parts of the body, which subsided by the fifth day. Fisichella (Riforma Medica, May 22, 1911).

An intravenous injection of 0.3 Gm. of salvarsan in a middle-aged patient was followed at once by cyanosis and nausea. The face swelled enormously and the tongue became too large to pass between the lips. There was intense headache and retching. The symptoms subsided after twenty minutes except for the swelling in the face. By the next morning nothing was left of the disturbances but moderate edema of the eyelids. The pulse and temperature had been persistently normal. Levin (Med. Klinik, May 28, 1911).

Case of a man, 46 years old, who came under treatment about three months after infection. Wassermann reaction negative. He received 0.4 Gm. of salvarsan, which was well borne. Four days later, 0.4 Gm. of salvarsan was again given intravenously, but this time it was followed by fever, tendency to vomit, diarrhea, and a marked exanthem. Four days later there was a spastic paraparesis with disturbances of the bladder and rectum, and anomalies of sensation. Juliusberg and Oppenheim (Münch. med. Woch., July 18, 1911).

Three days after the intravenous injection of salvarsan a patient became unconscious, with complete loss of all reflexes and sensibility. This condition lasted for three days, when it subsided gradually. Mann (Münch. med. Woch., Aug. 1, 1911).

Epileptiform convulsions followed an intravenous injection of salvarsan four months after a subcutaneous injection of the same drug. The patient was a robust butcher of 29. Consciousness did not return and the clonic cramps continued with delirium until death occurred from aspiration pneumonia. The symptoms developed three hours after the injection of salvarsan. Necropsy failed to disclose any satisfactory explanation of the case. Kannengiesser (Münch. med. Woch., Aug. 22, 1911).

A man syphilitic since six months demanded insistently to be treated with salvarsan, although an injection of 0.6 Gm. previously administered elsewhere had induced after four days coma lasting forty-eight hours and loss of memory persisting a week. The author was able to give this patient successive doses of 0.2, 0.3, 0.4, and 0.3 Gm. without causing any untoward effect except slight jaundice after the last dose. Among the most severe untoward phenomena seen from salvarsan by the author were jaundice lasting three weeks in 3 cases and thrombosis of veins of lower extremity in 2 cases,—1 an obese woman with varicose veins and the other an aged man. Milian (Bull. méd., Nov. 29, 1911).

The exanthemata observed after salvarsan injections are cases of idiosyncrasy, produced through accumulation of arsenic, that is, an artificial idiosyncrasy, while inborn idiosyncrasy is not observed. Cutaneous vaccination as a test before salvarsan or neosalvarsan treatment is useless. Zieler (Münch. med. Woch., July 23, 1912).

Report of 2 cases that gave marked clinical evidence of liver disease simulating acute atrophy after salvarsan and at the autopsy showed marked degenerative changes in the liver. The changes in 1 case were due to the arsenic, but in the other probably to endotoxins from the spirochetæ. The more recent areas of degeneration in the liver contained arsenic in the first case, but this was lacking in the other, in which syphilis therefore could not be excluded as the cause of death. Severin and Heinrichsdorff (Zeit. f. klin. Med., Bd. lxxvi, S. 138, 1912).

A few patients appear to have an absolute idiosyncrasy for salvarsan. For every other individual there is a *tolerable dose* which may safely be given. The signs of intolerance to salvarsan may be classified into marked and slight. The former are easily recognized: intractable vomiting, a scarlatiniform erythema, jaundice, etc. The latter comprise (*a*) gustatory sensations, (*b*) various glandular secretions. The first consists of a taste of ether, or of salt, a slightly alliaceous flavor which is experienced by the patient at the very commencement of the injection, sometimes even after only 2 or 3 c.c. of the liquid have been injected. At the moment when the taste is felt, the pulse will often be found to be slowed. Neosalvarsan causes the same phenomenon, but less frequently. During the injection a hypersecretion of certain glands may also be noted, especially the lachrymals. The patient sniffs slightly and then his eyes run with water. This secretion may continue for several days after the injection. A salivary hypersecretion may also be observed, causing the patient to expectorate as though chewing tobacco. It is probable that this action of salvarsan is connected with its vasodilator properties. Other glands, such as the intestinal, the liver, the pancreas, and the ovaries may be influenced in a similar manner. Milian (Paris méd., No. 49, 1912).

A man who had been infected with syphilis three years before presented the first symptoms of a fatal softening of the spinal cord fifty-six hours after an injection of salvarsan. Newmark (Amer. Jour. Med. Sci., Dec., 1912).

Report of 4 cases in which a sudden drop in the pulse rate, with partial syncope, was observed to take place, in two instances during injections of salvarsan, and in the others during ordinary blood-pressure estimations with the Riva-Rocci instrument. In all recovery soon took place. In the first 2 cases, in which the psychic factor could be ruled out, since the untoward phenomena appeared only at the close of the injection, the disturbance was attributed to a direct action of the drug on the pneumogastric centers; in the other patients, who complained of pain during the inflation of the blood-pressure cuff, the bradycardia may have been reflex. J. Schwartzmann (Semaine méd., Jan. 22, 1913).

Repeated injections of salvarsan are more likely to cause toxic effects than a single injection, apparently owing to accumulation of the drug or its products in the system.

It has been repeatedly noticed that where other pathogenic micro-organisms than the spirochete are present the toxic effects are more marked than usual. Thus, as stated by McDonagh, an injection of salvarsan in a patient with septic tonsillitis or influenza will cause an uncommonly pronounced reaction, and may aggravate the disorder present. In the same way, a latent bronchitic process may be excited to renewed activity by salvarsan. Epileptiform seizures have been known to follow the administration of the drug in patients predisposed to such disturbances.

> Case of amebic liver abscess in which, five days before operation, 0.4 Gm. of salvarsan was given intravenously. The patient at once reacted with a rise of temperature to 42° C. (105.8° F.), then showed alarming collapse with subnormal temperature. Though he had given many hundred salvarsan injections the author had seen no similar occurrence. O. Müller (Arch. f. Schiffs- u. Tropen- Hyg., May, 1913).

Anaphylactoid phenomena occasionally occur at a brief interval after an injection. The general blood-pressure falls and the intracranial pressure rises. The treatment in such cases should consist of immediate lumbar puncture, to relieve the high intracranial tension; saline enteroclysis or intravenous infusion, and the administration of caffeine hypodermically and magnesium oxide by the mouth.

> Besides the toxic effects sometimes observed with the first injection of salvarsan, which can be attributed to non-sterile solutions, certain phenomena are sometimes observed after repeated injections which resemble acute anaphylaxis. These attacks appear usually only after from 30 to 50 c.c. of solution have been introduced. The patient has an anxious look, complains of pressure in the gastric or cardiac region followed by a sense of suffocation; later there is a bright-red suffusion of the face and sometimes the whole body, occasionally changing to a purple cyanosis. In marked cases the eyelids and lips appear swollen. This may occur at any stage of the disease. In 1 case there occurred a toxic erythema. Guinea-pigs sensitized by the injection of a mixture of guinea-pig serum and salvarsan, and which have been reinjected after a suitable time with the same mixture, show symptoms like those seen in anaphylactic shock. It would seem that salvarsan has so altered the native serum that it acts like a foreign proteid. It is probable that similar phenomena may occur in the human subject. H. S. Swift (Jour. Amer. Med. Assoc., Oct. 5, 1912).
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> He who administers salvarsan should be prepared with the needful apparatus for enteroclysis, lumbar puncture, and intravenous saline injection, since anaphylactoid phenomena may call for emergency treatment. Edward Martin (Penna. Med. Jour., Nov., 1912).

Herxheimer's reaction consists of a prompt but temporary aggravation or greater prominence of a syphilitic skin eruption present at the time of the injection. The phenomenon is devoid of any unfavorable significance, probably signifying that the drug has caused transient increased activity of the spirochetes, just as, *e.g.*, atoxyl will cause augmented motility of the trypanosomes before they succumb to its toxic action in the sleeping sickness. Where, however, as is sometimes the case, the Herxheimer reaction appears not immediately but a few days after the injection, the cause is probably the toxins set free by the destruction of the spirochetes.

Morbilliform eruptions, urticaria, herpes zoster, and angioneurotic edema have also been observed to follow salvarsan, generally about a week after the injection.

> Case of a male, aged 22 years, suffering from secondary syphilis with slight glandular enlargement and syphilitic orchitis. He was given 0.6 Gm. of salvarsan intravenously. Two days later a typical measles eruption developed. The attack pursued a mild but typical course. L. L. Williams (Boston Med. and Surg. Jour., May 16, 1912).

The so-called *"neurorecurrences,"* consisting of the appearance in syphilitic patients of evidences of paralysis of one or more of the cranial nerves, especially the auditory and optic, have been fairly definitely shown to be due almost always to the syphilitic process itself, and not, as for a time seemed plausible, to direct or indirect effects of the salvarsan itself. This is indicated by the marked improvement which occurs after further treatment by salvarsan or mercury. As McDonagh observes, neuritis of cranial nerves after salvarsan almost always occurs in patients in the early secondary stage of syphilis, the Wassermann reaction being generally negative, and only one injection of the remedy having been given. Apparently the reason for the sudden widespread interest aroused in "neurorecurrences" is that the introduction of salvarsan led, in conjunction with the observations of its effects on the disease, to a much closer study of early syphilitic involvement of the cranial nerves and to a realization of the fact that the gradually developing lesions of this kind are far more frequent accompaniments of the disease than had previously been supposed. On the whole, cranial nerve trouble merely implies insufficient treatment. Where series of salvarsan injections are given, such a condition is rarely seen.

> Nerve recurrences are not due to a toxic action of salvarsan, but are clinical symptoms of a swelling induced by the pathological process, because: (1) The interval between the injections and the onset of the nerve manifestations is considerable. (2) The cause of the recurrence seems to be an irritation or inflammation of the nerve, as is particulary shown in the affections of the optic nerve. On the contrary, other arsenical preparations seem to cause an atrophic condition of the nerves. (3) The recurrences seem to appear almost exclusively during a certain period of syphilis. (4) Such recurrences have not been observed in non-specific diseases treated with salvarsan. (5) These recurrences are cured by specific treatment, particularly by renewed treatment with salvarsan. (6) The recurrences appeared in most cases after the smaller doses of salvarsan. (7) These same symptoms have been observed under mercurial treatment. Chancres about the head are particularly inclined to result in nerve recurrences. Certain prodromal symptoms may indicate a nerve recurrence, such as headache, dizziness, ringing in the ears, or some disturbances with vision, and patients should be instructed to report for further treatment in the advent of any such symptom. Benario (Münch. med. Woch., Bd. lviii, S. 732, 1911).
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> Case of a young man given two intravenous injections of salvarsan in the fourth month after infection. These were followed two months later by multiple paralysis of cranial nerves. There was total deafness on the left side, with the characteristics of a true syphilitic affection of the

auditory nerve on this side, while on the right side the symptoms indicated a toxic injury of the right auditory nerve. A woman of 28 developed weakness and paralysis in the domains of the first, sixth, seventh, ninth, and eleventh cranial nerves two months after an intragluteal injection of salvarsan, and as these phenomena subsided signs of mild polyneuritis became evident. There has been improvement during the six months since, but certain symptoms still indicate meningitic irritation. A third case suddenly developed crossed hemiparaplegia which gradually improved under mercurial treatment. An intramuscular injection of 0.3 Gm. salvarsan was then made. Eight days later the signs of peripheral polyneuritis became evident and persisted with little improvement for three months. Frömmer and Delbanco (Münch. med. Woch., Sept., 1911).

A case of secondary syphilis with vision and fundi normal received 0.275 Gm. and twenty-five days later 0.5 Gm. of salvarsan intravenously. Five weeks later, patient reported vision had been failing for one week. Fundus: neuroretinitis. Patient put on mercury treatment, which was continued three months, during which time vision gradually became less until it was $^{20}/_{100}$ in each eye. Intervening examinations at times indicated an improvement, but the condition would again relapse. Then 0.3 Gm. of salvarsan was given intravenously. Vision improved rapidly, while the neuroretinitis was rapidly clearing up. This was not the course one sees following neuroretinitis in latent syphilis, or from the toxic action of any of the drugs, but was the usual condition from repeated injections of salvarsan in such cases. E. R. Carpenter (Laryngoscope, Sept., 1912).

Report of 3 cases in which choked disk developed in an extreme form after one or two injections of salvarsan. Neurorecurrences have certainly become much more frequent since salvarsan has been used. The author has never known nor heard of such extreme forms of choked disk in syphilis as he saw in these cases. Vollert (Münch. med. Woch., Sept. 3, 1912).

Nerve relapses are the manifestation of a monorecurrence at a point inaccessible to the medication. Every day of postponement of vigorous treatment reduces the prospect for complete restitution. Not the severity of the case should be accepted as the criterion for mercury or salvarsan treatment—the question is whether it is possible to put through a vigorous course of salvarsan treatment. Unless the patient is able and willing to take the two or three weeks' intensive course, it is better to refrain from salvarsan altogether. Benario (Münch. med. Woch., Oct. 1, 1912).

Report of 9 cases of neurorecurrence after salvarsan. Examination of the cerebrospinal fluid confirmed the belief that these are merely a manifestation of the disease and that salvarsan has nothing to do with them. Prompt subsidence of the symptoms occurs under continued cautious use of salvarsan. In 1 case an intravenous injection of 0.2 Gm. of salvarsan transformed in two days the alarming clinical picture: convulsions, unconsciousness, vomiting, pulse 96 to 118, temperature normal. This syndrome had developed suddenly two months after two injections of salvarsan. The auditory apparatus was the seat of the neurorecurrence in the other cases except in 1, in which intense headache was the only symptom. All these patients recovered under continued use of the salvarsan or under mercury. Assmann (Berl. klin. Woch., Dec. 16, 1912).

About a month after an intravenous injection of 0.6 Gm. of salvarsan a patient had a severe attack of giddiness with impairment of hearing, which was reduced to watch at four inches in the right ear and contact in the left. The left side of the face was slightly flat. The giddiness increased under potassium iodide alone, but was improved by pilocarpine hypodermically and purgation. The patient was kept on iodide all summer and his hearing improved to watch three inches in each ear with slight response to caloric tests. Equilibrium is still disturbed, but the slight facial paralysis has disappeared. C. A. Clapp (Jour. Amer. Med. Assoc., March 8, 1913).

Deaths from salvarsan have in the great majority of cases occurred either where contraindications have been disregarded; where the drug has been given as a last resort, with but little hope that it would bring about recovery; or where the technique followed has been faulty or a manifestly excessive dose given. Wechselmann, at the close of his monograph on salvarsan fatalities, emphasizes the fact that these cases present no definite type—except, perhaps, the group of those succumbing to hemorrhagic encephalitis—and can, therefore, not be collectively discussed or explained. He considers renal insufficiency, however, and not abnormal sensitiveness of the brain-centers, the essential condition predisposing to salvarsan death. Accumulation of arsenic in an organism in which the viscera are normal functionally cannot be considered a cause, as Wechselmann has given doses of 0.6 Gm. ten to fifteen times at intervals of but two or three days without witnessing any ill effects, whereas in many of the fatal cases only 0.3 to 0.8 Gm. had been given altogether. Neither can idiosyncrasy be said to account for salvarsan fatalities, for in many instances death has been produced not after the first but the second or a subsequent injection. Again, the morbid phenomena witnessed in these cases before death do not correspond with those of arsenic poisoning.

Case regarded as a fatal toxic encephalitis following injection of salvarsan in a robust army officer, 33 years old, seven years after infection with syphilis. He had taken systematic, intermittent courses of mercury for five years. The dose of 0.6 Gm. of salvarsan was injected into the gluteal muscle without apparent local reaction. Over two months later complete loss of appetite and slight nausea developed, with general weakness, soon followed by disturbances in vision and vertigo. The Wassermann reaction was negative. Symptoms of encephalitis became evident and a sausage-shaped resistant patch could be felt in the gluteal muscle and was excised; large amounts of salvarsan and arsenic were found, but there was no striking necrosis. Vigorous mercurial and iodide treatment was instituted, but the symptoms indicating encephalitis continued and the patient died. No necropsy. Ehrlich points out that the assumption of a toxic affection prevented the vigorous antisyphilitic treatment which should have been instituted earlier, and which might have saved the patient if the trouble had been, as he surmises, merely a recurrence of active syphilis. Intramuscular injection of salvarsan is inadequate. Hrdliczka (Wiener klin. Woch., May 25, 1911).

A woman of 33 had never taken treatment for her syphilis, until 0.4 Gm. of salvarsan was injected in the gluteal muscles. Seven hours afterward there was sudden trouble in breathing, soon leading to complete arrest, which proved permanent notwithstanding artificial respiration for an hour. The necropsy findings indicated recent syphilitic meningitis with true tabes. The fatality was evidently due to sudden paralysis of the phrenic nerve from pressure from the hyperemia and edema in the spinal canal induced by the action of the drug—all the regional tissues, including the phrenic nerve, being already pathological from the syphilitic disturbances. This harmonizes with the frequent experience of neuropathologists that nerves suffering from toxic, infectious or other injurious influences are peculiarly liable to become paralyzed even from some slight injury such as moderate pressure. If the necropsy had been omitted and the pre-existing, clinically latent inflammation of the phrenic nerve had not been discovered the fatality might have been ascribed to the toxic action of the drug alone. A. Westphal (Berl. klin. Woch., May 29, 1911).

A man of 32, six years after infection, was given an intravenous injection of 0.6 Gm. salvarsan. Symptoms of gastric and brain disturbances appeared on the second and third days, and at necropsy, six days after the injection, the brain showed traces of acute hemorrhagic encephalitis, the blood escaping by diapedesis as in infectious processes. The brain may have been peculiarly sensitive in this patient, as he had had much worry and sought recreation and relief from insomnia in distractions of varied kinds. Almkvist (Münch. med. Woch., Aug. 22, 1911).

Case of a physician, 40 years old, who had contracted syphilis in his professional work, the primary sore being in the nose. He was given an intravenous injection of 0.4 Gm. of salvarsan, followed by thirty mercurial inunctions. After an interval of five days—forty days after the first injection of salvarsan—the same amount was injected again. Two and a half days afterward he suddenly became deeply comatose and cyanotic, and died with progressive symptoms of heart-failure.

Autopsy was held and disclosed parenchymatous degeneration of the organs, but no real cause of death was apparent until microscopic examination showed an acute encephalitis. B. Fischer (Münch. med. Woch., Aug. 22, 1911).

Deaths occurring in hopeless cases—big aortic aneurisms, severe cardiac disease, advanced tuberculosis, or terminal stages of pernicious anemia—cannot be laid at the door of salvarsan. In these cases minimal doses (0.1 Gm.) should be used. Cases which die with symptoms of encephalitis hemorrhagica, on the other hand, are most likely due to edema resulting from too rapid death of the spirochetes. These accidents can be avoided if all syphilitics who show early brain symptoms are treated with very small doses given at intervals. Complete rest after the injection is strictly indicated. Cerebral pressure symptoms then occurring must be relieved by spinal puncture or even by decompression. Salvarsan is relatively harmless—more so than chloroform, for example; 2 to 3 Gm. can be given in the course of a few weeks. P. Ehrlich (Münch. med. Woch., Nov. 21, 1911).

Report of 2 cases of death after salvarsan. The first, observed by Oltramare, was that of an obese man of 48, syphilitic since 15 years, presenting no evidence of renal or cardiac disturbance or of spinal or brain involvement, who succumbed, after a period of coma, three days after an intravenous injection of 0.6 Gm. of salvarsan in alkaline solution. The autopsy showed leptomeningitis, fatty degeneration of the heart, chronic purulent bronchitis, and bronchopneumonic lesions in the lower lobes of the lungs. Caraven brought to the author's notice the case of a young man of 21, without organic lesions of any kind, who died similarly four days after a second injection of 0.6 Gm. of salvarsan, the first having been given a week previously. The autopsy showed marked congestion of the brain and lungs, reddened and soft kidneys, and hemorrhagic foci in the stomach lining. Gaucher (Bull. de l'Acad. de Méd., Nov. 21, 1911).

Case of a man of 30 with severe convulsions developing on the third day after a second injection of salvarsan. The convulsions returned at intervals, with unconsciousness, deviation of the eyeballs, clonic and tonic muscular spasms, and abolition of the pupillary reflex. In the intervals the mind was clear and the reflexes normal, but the man complained of intense headache. He died in coma the second day after the onset of the convulsions. The necropsy findings indicated a severe acute action on the central nervous system and kidneys of some toxic agent. The salvarsan seemed to have contributed directly or indirectly to bring about the fatality in this case. The symptoms did not resemble those of arsenic poisoning; there were no gastrointestinal disturbances, but the syndrome was identical in every respect with that in the "salvarsan fatalities" on record. The necropsy findings also showed numerous analogies with those of arsenic poisoning. Assmann (Berl. klin. Woch., Dec. 16, 1912).

Case of a girl of 11 with parenchymatous keratitis from inherited syphilis. After vigorous mercurial treatment vision improved and the general health was good, but the Wassermann reaction was still strongly positive. Fifty-four inunctions had been made in sixty-nine days, but the persisting Wassermann reaction showed that the causal germs were resistant to mercury and the author changed to neosalvarsan, giving an intravenous injection of 0.4 Gm. (corresponding to 0.266 of salvarsan). Fifteen minutes later the child developed slight and transient nausea, chilliness and headache, but she felt so well by evening that she went out. Three days later a second injection was given of 0.75 Gm. neosalvarsan (equal to 0.5 Gm. salvarsan). The bowels failed to move for three days; nausea and headache developed, followed by a sudden onset of symptoms of an acute affection of the brain, and the child died within twenty-four hours. The necropsy findings were negative, nothing pathological being found except a slight tendency to fatty degeneration of the liver. The features of the case also exclude anaphylaxis, and they did not correspond to the picture of arsenic poisoning. The severe brain and spinal-cord symptoms can be explained most plausibly by Ravaut's "cerebrospinal reaction," evidenced by the appearance of albumin and lymphocytosis in the cerebrospinal fluid. Ravaut found this cerebral reaction in the secondary stage of syphilis; but in the author's case the disease was of the hereditary type. Schestopal (Berliner Klinik, April, 1913; Jour. Amer. Med. Assoc., June 21, 1913).

Wechselmann, collecting accounts of all or nearly all the post-salvarsan fatalities—in adults only—recorded up to the fall of 1912, cites 6 cases occurring after subcutaneous and 15 after intramuscular injection, and points out the fact that in none of these can the accident be considered due directly to poisoning by the drug itself.

Among the much more numerous cases occurring after intravenous injection, Wechselmann lists 25 in which either the injection was given with the patient already *in extremis,* gross errors of technique were made (such as failure to alkalinize relatively concentrated solutions), or serious lesions of various organs existed fully accounting for the fatal result, *e.g.,* tuberculosis, syphilitic meningitis, aneurism, sclerotic changes, cancer, etc. Another series of 10 cases comprises those in which the power to excrete the drug was impaired owing to the effects of chronic alcoholism, syphilis, and mercury on the internal organs. Twenty-five more cases were due to the presence of nephritis; in a large proportion of these anuria and uremic phenomena were noted; in some the renal changes were apparently slight. In both this and the preceding group, combined salvarsan and mercurial treatment had been administered. The remaining—much smaller—groups include the cases neither subjected to combined treatment nor presenting albuminuria, those dying of acute yellow atrophy of the liver (probably quite independently of the salvarsan), and those suffering from severe diseases other than syphilis, and free of the latter.

A pale, slight man, with syphilitic plaques on the tongue, lips, and several enlarged glands, was ordered biniodide of mercury injections, which were badly borne, and subsequently injections of 40 per cent. gray oil. A year later the glands of the neck were found much enlarged and plaques in the mouth evident. Weight 43 kilos (94 pounds). No albuminuria. No lesion in the heart or lungs. Three hours after an intravenous injection of 0.4 Gm. of salvarsan in alkaline solution, vomiting, diarrhea, and sweats supervened. The vomited matter was greenish and at times mixed with dark blood, the diarrhea abundant and frequent, perspiration copious, and palpitation violent. The lips were violet, the tongue chocolate and dry, the aspect very pale, temperature 36° C. (96.8° F.), radial pulse almost imperceptible. On the two days following the injection, until he died, the patient did not pass a single drop of urine, and the bladder was entirely empty. E. L. Morata (Rev. de med. y cir. pract., Feb. 28, 1911).

A patient received 0.5 Gm. (7½ grains) of salvarsan by vein and after the injection complained of severe abdominal pain. For three days she voided no urine; on the fourth, however, she passed three ounces of clear urine; from then until death on the following day she passed no more. She died in coma. On microscopic examination of the liver the parenchyma cells in the central part of the lobules were quite irregular in size and shape and had ragged, indistinct margins. Many contained a bright-yellow pigment and all showed vacuoles. The protoplasm was granular and the nuclei of different sizes and shapes, some scarcely distinguishable. Some of the cells contained three or more nuclei, suggesting direct division. Some cells showed mitotic figures in various stages. In the kidneys proliferation of the epithelium was present in all parts of the convoluted tubules. Polynuclear cells were common. Occasionally syncytial, budlike masses of protoplasm were found. There was an excessive amount of desquamation of the epithelial cells. There were no evidences of severe vascular injury, such as is common after arsenical poisoning. H. O. Ruh (Cleveland Med. Jour., Sept., 1912).

Two fatal cases observed following salvarsan. The first was a man, 30 years of age, who received three intravenous injections of 0.6 Gm. each within a period of two months. The first two injections were given two days apart. He also received an injection of metallic mercury. Within a few hours after the third injection of salvarsan there was a slight tingeing of the scleræ and on the following day universal icterus, terminating fatally after four weeks, with the picture of an acute yellow atrophy of the liver. Chemical examination of the liver and spleen gave a definite arsenical mirror.

The second case occurred in a woman of 29 years who had received mercury injections repeatedly. Within two months she received four injections of salvarsan—two intravenously and two intragluteally—the combined dosage being 1.95 Gm. About seven months after the last injection of salvarsan icterus set in, which ended fatally within eighteen days, with the picture of acute yellow atrophy and ascites. Only faint traces of arsenic could be detected in the liver. The pathologicoanatomical diagnosis was chronic yellow atrophy of the liver. In the second case the condition did not follow soon after the salvarsan was injected, and the concurrence of syphilis as a cause could not be ruled out. Severin and Heinrichsdorff (Zeit. f. klin. Med., Bd. lxxvi, 1912).

While recognizing the frequency of brain symptoms in cases of death after salvarsan, Wechselmann, as the result of his comprehensive study, feels impelled to lay most stress upon failure of elimination as the cause of these symptoms. Although the fact that salvarsan may be well borne even by seriously diseased kidneys, but may cause death where the histological changes are slight, would seem to be in opposition to the above view, the work of Schlayer has shown that disturbances of renal function in general by no means necessarily parallel the actual, evident pathological changes present. Moreover, Wechselmann points out that arsenic has been demonstrated to impair, even after small doses, the ability of the renal vessels to dilate or contract—thereby tending to arrest the kidney function—while mercury induces essentially a tubular nephritis, with albuminuria and casts. Since nearly all the cases of salvarsan death in robust individuals have shown the combination of energetic mercurial treatment with intravenous administration of the arsenical remedy, Wechselmann is inclined to consider this association responsible for a number of the deaths from salvarsan recorded. That such is actually the case is indicated by a rather extensive array of experimental and clinical evidence, which makes it seem probable that in persons whose kidneys are unusually susceptible to the effects of mercury, and are therefore somewhat disturbed in function even by ordinary mercurial treatment, the added paralyzing influence of the arsenic in salvarsan on the renal vessels will be sufficient to arrest the renal function. This, in turn, will cause retention of the salvarsan in the system for an unusual period, and a considerable amount of it will become oxidized, forming a compound far more toxic than salvarsan. (Ehrlich himself agrees with Wechselmann that this oxidation in the system may be increased owing to stasis brought on by kidney insufficiency.) Finally, since several observers have noted that salvarsan exposed to the air was particularly likely to bring on anuria, the readiness with which death may occur through the mechanism advanced by Wechselmann will without difficulty be realized.

Comparison between the effects of toxic doses of salvarsan and of bichloride of mercury. Salvarsan has a relatively slight effect upon the kidney and a relatively marked effect upon the liver; about three times as much arsenic will lodge in the hepatic cells as will be found in the renal epithelium. As is well known, bichloride of mercury attacks the kidney with great avidity, so that the organ is rapidly damaged; on the contrary, its action upon the liver is relatively slow and slight, the action in each case bearing a direct relationship to the amount of the drug. Oettinger and Fiessinger, examining a case of poisoning by intramuscular injection of mercury, discovered 0.01 Gm. of mercury for each 1000 Gm. of liver tissue, while three times as much was found in the kidneys. Morel, Mouriquand, and Policard (Jour. de phys. et path., July 15, 1912).

Case of a woman with ulcerative syphilitic lesions of the throat and labia, previously treated with mercurial inunctions. Urine clear and free of albumin; specific gravity 1014. The ulcers recurring, an injection of 0.6 Gm. of neosalvarsan was given, which was well borne. Eight days later another injection of the same dose was given. Two days after, a slight tremor appeared and the knee-jerks became exaggerated. Next day, convulsions, unconsciousness, and cyanosis; followed, a day later, by coma, marked cyanosis, and death. The autopsy revealed a cloudy condition of the epithelium of the convoluted tubules. The cells of Bowman's capsule surrounding the glomeruli were in part thickened, swollen, and detached. Busse-Merian (Münch. med. Woch., No. 43, 1912).

Case of syphilis in the secondary stage in which seven injections of calomel had been given, stomatitis appearing after the fifth. Some albumin in the urine was also noticed. Nine days after the last mercurial injection 0.5 Gm. of neosalvarsan was given intravenously, two days later 0.9 Gm., and in two days more 1.08 Gm. At least seven hours later a mild febrile reaction was noted—38.5° C. (101.3° F.). Next morning the temperature was normal, but some general depression experienced. In the afternoon convulsions and unconsciousness supervened. Venesection and intravenous saline infusion brought about some improvement, but next morning the convulsions recurred and the patient became cyanosed.

Death took place notwithstanding the use of artificial respiration. The post-mortem examination showed thrombosis of the left ulnar vein; embolism of the pulmonary artery; marked parenchymatous degeneration of the renal epithelia in the convoluted tubules, with advanced nuclear necrosis. There were no perceptible changes in the brain. The author considers the case one of retention intoxication due to renal insufficiency. Gennerich (Praxis der Salvarsanbehandlung, p. 20, 1912).

The retention of salvarsan in the blood destroys the oxygen-carrying property of the latter, and deaths after the use of the drug are the result of a severe kidney lesion. Therefore, every salvarsan injection demands the minutest control of the kidney function. Antoni (Deut. med. Woch., March 13, 1913).

Unsuspected abnormal conditions of the heart have been held responsible for death after salvarsan. Thus, Martius reports 7 cases of death by heart-failure occurring at a varying interval after the administration of salvarsan, although symptoms and physical signs of cardiovascular disease had been either absent or present only in slight degree. At autopsy 5 of these cases presented syphilitic aortitis, coronary sclerosis, and myocarditis, and 1 a hypoplasia of the heart and aorta. Wechselmann points out, however, that salvarsan does not in itself seem to be injurious to the heart (this has been clearly established in regard to the normal heart) and that in patients suffering from cardiac disease, especially in arteriosclerotics, it is, as a rule, very well borne, generally even improving syphilitic hearts. In cases like those reported by Martius, as well as in instances of cardiac or renal hypoplasia in general, he considers the risk of salvarsan injections to reside at least in part in the accompanying diminished capacity of elimination. The same probably applies to the use of salvarsan in cases suffering from febrile affections.

Guinea-pigs were injected with "606" in doses ranging from 0.009 to 0.12 Gm. per 100 Gm. of body weight and succumbed in one to thirteen days. In those that died in twenty-four hours (dose 0.01 to 0.012) the organs were intensely congested and contained hemorrhagic foci. The liver was enlarged, the blood-vessels engorged, the trabeculæ were compressed, and the hepatic cells around the portal radicles were infiltrated with fat; the kidneys were congested, especially in the cortex; interstitial and intralobular hemorrhages and a small cortical infarct were also observed. The spleen was greatly congested; the Malpighian corpuscles were hypertrophied and infiltrated; the large white cells were increased and filled with blood-pigment. The suprarenal glands showed medullary engorgement. The myocardium was congested. The lungs presented basal congestion and subpleural lobular hemorrhages. The intestines were filled with diarrheal material. In the animals that died on the fourth day, similar changes were found. Those that lived nine to thirteen days were affected to a slighter degree. Gaucher (Bull de l'Acad. de Méd., Nov. 15, 1910).

A man had well-compensated mild aortic insufficiency, but no other pathological findings were detected in the heart. A few days after subcutaneous injection of 0.3 Gm. salvarsan, signs of heart weakness appeared, proving fatal on the eleventh day. Necropsy revealed unsuspected degeneration of the myocardium, which had evidently been aggravated. Spiethoff (Münch. med. Woch., Jan. 24, 1911).

Local Untoward Effects.—Intramuscular injections of salvarsan in some instances cripple the patient for a number of days. An indurated mass may be produced which remains for months, and even, in rare instances, local softening and evacuation of sterile pus may take place. Intense pain may be present for as long as a week. The swelling, which begins about the third day, generally does not *per se* give rise to pain, and subsides, for the most part, at the expiration of a week, only to be replaced, in many instances, by the induration already referred to. Heat and cold may be alternately applied to relieve any discomfort present, or, if the skin area becomes hyperemic, lead water and laudanum may be used. Fluctuation does not indicate incision, but at most aspiration, as the fluid present is sterile.

Abscesses after intramuscular injection result from one of three causes: improper preparation of the solution or suspension employed, insufficiently deep injection of the drug, and bacterial contamination. Examination of the walls of one of the cavities showed an increase of fibrous tissue, with complete blocking of the smaller vessels and lymphatics by minute particles of salvarsan. Numerous small masses of the substance were also found in pocket-like cavities distributed through the section. There were degenerative changes, with decrease in amount of both connective and elastic tissue. In the immediate vicinity of the lesion evidence of inflammation was almost entirely lacking, and round-cell infiltration was conspicuous by its absence. Probably the drug, which had been employed in a supposedly alkaline solution, had not been completely dissolved. In treating these lesions it is best to dissect or curette out the lining of mummified tissue and allow the cavities to fill up by granulation. Balsam of Peru, with an occasional application of copper sulphate or powdered alum, is of value. When the healing process is well established recourse may be had to an 8 per cent. scarlet-red ointment. R. L. Sutton (Boston Med. and Surg. Jour., Dec. 21, 1911).

Extensive necrosis occurs only after subcutaneous injection. The tissues become transformed into a brownish mass, surrounded by a fibrous capsule. Such necrosis may be avoided by injecting the salvarsan at several points rather than in one locality alone. It occurs oftener if the drug is administered in the thoracic region than in the gluteal (McDonagh).

> Case of thrombosis after intravenous infusion of salvarsan. By accident, the injection was made elsewhere than in the area sterilized for it. The patient was a young man who had had veins punctured for the Wassermann test five times and also for a second infusion of salvarsan, without mishap. The thrombosed vein was resected a month after the infusion, and the *Streptococcus albus* was cultivated from it. Hausmann (Münch. med. Woch., Dec. 13, 1910).
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> Local reaction after the intravenous method means one or several of the following: (1) Infection. (2) Injection of the fluid into the circumvascular cellular tissue. (3) Penetration and injection of the wall of the vein. (4) Transfixion of the vein and injection into the sublying tissues. (5) Too rapid injection. G. F. Lydston (N. Y. Med. Jour., Oct. 21, 1911).

Untoward Effects from Neosalvarsan.—Experience with the newer form of the Ehrlich-Hata remedy seems to have shown that it is in many respects less likely to produce untoward results than the older compound, provided certain contraindications and details of technique be borne in mind, and the injections not given at unduly short intervals. Thus, Bayet states that fever, nausea, vomiting, headache, and general lassitude are less often observed with the new remedy. Stühmer calls attention to the fact that intestinal disturbances and collapse are almost never witnessed with it, although drug rashes are more frequent. Kerl and Schreiber confirm these observations. Rytina found, upon giving intramuscular injections of neosalvarsan, that evidences of a general reaction were limited to a few, in which there was a slight transient nausea and a rise of the temperature up to 99.4° F. McIntosh and Fildes saw no immediate symptoms except diarrhea, though what they term a "spirochete fever," occurring in occasional cases several hours after the intravenous injection, was associated with nausea and vomiting. This fever they do not regard as an expression of the toxicity of the drug, but rather as a syphilitic anaphylactic phenomenon. Schreiber notes that the exanthemata sometimes following full doses of neosalvarsan occur between the eighth and the twelfth day.

> The authors have seen no symptoms follow the injection of 1.5 Gm. of neosalvarsan excepting diarrhea in some cases, unassociated with malaise. Nausea or vomiting apart from such occurring with the "spirochete fever" was absent. The fever sometimes occurring several hours after an injection of salvarsan, especially in tertiary cases, is still observable after neosalvarsan. Such fever is not an expression of the toxicity of the drug, but is perhaps rather a syphilitic anaphylactic phenomenon comparable to the fever following the injection of old tuberculin. J. McIntosh, P. Fildes, and H. B. Parker (Lancet, July 13, 1912).

A few observers appear to have dissented from the view that neosalvarsan is less often followed by toxic effects than salvarsan. Wolff and Mulzer concluded that it is much more poisonous, having observed headache, vomiting, and diarrhea in 14 cases out of 30, a chill in 1 case, extensive eruptions in 4, herpes labialis in 2, and nephritis, paralysis, and other serious phenomena in 1. Kall similarly enjoined caution in the use of neosalvarsan. Undoubtedly some of the earlier experiences with neosalvarsan were rendered unduly unfavorable owing to the attempts made to give doses larger than those corresponding to the standard amounts of salvarsan, and also to administer them at very short intervals. Ehrlich himself, collecting and analyzing all new literature on the subject, expresses a decided preference for neosalvarsan. One argument in its favor which seems to have been definitely accredited is the fact that untoward effects occurring after neosalvarsan generally follow the initial injection, so that the surgeon is warned as to what to expect on later occasions, whereas with salvarsan the more serious toxic effects have been manifested frequently after the second or subsequent injections.

Report of toxic effects, including some deaths, after salvarsan and neosalvarsan: (1) Case of vertigo, headache, and unilateral deafness three months after three injections of salvarsan; after four injections of calomel the vertigo disappeared, but the deafness and headache remained. (2) Case of unilateral deafness three months after three injections of salvarsan. (3) Case of death six days after a third intravenous injection of salvarsan. The patient was a young man in robust health and the symptoms were retention of urine and coma. (4) Retention of urine, albuminuria, icterus, and uremic symptoms, which only yielded to bloodletting, in a healthy young man, who had had a chancre three months previously. (5) Fatal case in a young woman five months pregnant, who died, after convulsions and coma, two days after a second injection of neosalvarsan (0.6 Gm.). (6) Case of paraplegia occurring four days after an injection of neosalvarsan in a young girl with ocular lesions due to hereditary syphilis. Gaucher (Ann. des mal. vénér., July, 1912).

Two cases in which neosalvarsan caused severe angioneurotic symptoms, collapse, congestion, or acute swelling of the brain, with an exanthem. One patient had complained of headache and the pupils did not react alike, before the drug had been given. Two days after the second injection of neosalvarsan he became unconscious for five hours and had violent headache on rousing. Death of a girl of 18 after two injections of neosalvarsan. Necropsy revealed the changes characteristic of salvarsan and neosalvarsan intoxication. The only symptom presented by the patient had been the recurrence of nodules on the external genitals during the preceding eight months. The two injections of 0.6 Gm. neosalvarsan were given intravenously after an interval of eight days. Serious symptoms developed the day after the second injection, with death two days later. Simon (Münch. med. Woch., Oct. 22, 1912).

Case of a man who had been given three intravenous injections of neosalvarsan,—0.6, 0.75, and 0.75 Gm., respectively—at three-day intervals. Three days after the last injection, phenomena of brain congestion appeared. Complete recovery ensued in two days. Schreiber's method of giving the drug at short intervals is not permissible. The patient referred to was neuropathic and an inveterate smoker. Perkel (Ann. des mal. vénér., Nov., 1912).

Modes of procedure in which advantage is taken of the greater *immediate* tolerance of the system to neosalvarsan to inject excessively large doses of the latter are to be condemned, as untoward happenings have occurred as a consequence, some of which have been quite serious. Thus, the author reports a case in which the administration of 1.5 Gm. of neosalvarsan in two doses was followed by paraplegia, the condition later becoming so grave as to endanger the patient's life. Bayet (Presse méd., Dec. 7, 1912).

Two cases of fresh secondary syphilis in which, following the intravenous injection of 0.9 Gm. of neosalvarsan, a severe nephritis ensued. In 1 a pneumonia followed which proved almost fatal. The possibility of error in the preparation of neosalvarsan was practically *nil*. P. Wahle (Münch. med. Woch., Feb. 18, 1913).

Locally, neosalvarsan has been stated to cause less irritation than the older substance. Indeed, it is natural that a compound which can be given in a neutral, readily absorbable preparation should produce a less prolonged local disturbance than one which has to be given in an alkaline or acid solution, or in a suspension. Yet most observers who have tried out the intramuscular route in connection with neosalvarsan have abandoned it in favor of the intravenous procedure. Hazen states that one must be prepared for severe pain after administering salvarsan in either water or glycerin, and that he found injections of neosalvarsan in an oily menstruum to give more pain than where salvarsan was used.

THERAPEUTICS.—In Syphilis.— The effect of salvarsan in this disease is considered to be, at least in major part, a direct one upon the causative spirochetes. The remedy is intended to combine with the protoplasm of the parasites and kill the latter without affecting the cells of the host. McIntosh and Fildes have shown, in experimental work on rabbits, that the drug possesses spirocheticidal power far in excess of that of mercury. McDonagh refers to the fact that if scrapings from a chancre which is healing under salvarsan are examined before the spirochetes have entirely disappeared, the organisms will be found "swollen, broken up, and not so much curved, but with a swelling somewhere along their course,"—this swelling probably being analogous to a spore.

In experimental syphilitic testicular infection in rabbits the authors followed the effect of medication upon the spirochetes by means of darkground illumination. After injection of salvarsan the destruction of the micro-organisms began in about three hours and was complete in seven hours. In man the corresponding figure is nine hours after adequate treatment. Within two hours of injection pain over the lesion disappeared, since the animal no longer winced under the frequent examinations. In six hours the ulcer had shrunk so much that the scab appeared relatively too large. Mercury was given intravenously in the form of the iodide. The effect on the spirochetes was much less after two injections than after one injection of "606." No alteration was found twenty-four hours after the first injection, while even four days after a few spirochetes were found. On the fifth day, however, no organisms were detectable. The local effect was also much slower. The amount of "606" used represented only one-sixth of an adult human dose, while the amount of mercury represented three adult human doses. As to iodide of potassium, no effect on the spirochetes was observed and no alteration in the size of the lesion. McIntosh and Fildes (Lancet, Sept. 30, 1911).

With mercury the spirochetes are not killed *en masse*, but a great number are simply repressed and the natural defenses of the body are gradually brought to bear against the infection, and the patient goes more or less definitely through the various stages of the disease as if untreated. Even if he relapses he has the defensive asset in the mercury he has taken already. With salvarsan the great bulk of the spirochetes are killed at once and those that remain are too few to stimulate the resistance of the body and they begin again to multiply. Salvarsan has entirely upset the ordinary course of syphilis and introduced entirely new factors in the possibilities of serious relapse. Hence the advantages of the combination method. H. J. Nichols (Jour. Amer. Med. Assoc., March 2, 1912).

Action of neosalvarsan studied *in vitro* on *Spirochcta gallinarum, S. recurrentis,* and *Trypanosoma brucei.* After contact with the drug for periods of fifteen to sixty minutes all these parasites were still actively motile, but had lost their vitality; for when injected into animals they produced no infection. In order to eliminate the introduction of any of the drugs together with the parasites, the mixtures of neosalvarsan and parasites were centrifuged, by which means the latter were separated from the solution. Solutions of atoxyl had not this parasiticidal action *in vitro,* the parasites maintaining their virulence. These results show that there is a direct combination of neosalvarsan with the chemoreceptors of the parasites. G. Castelli (Zeit. f. Chemotherapie, 1 Teil. Orif., vol i, No. 2, 1912).

In the syphilitic tissues of man and in all the blood constituents of mice and rats thus far examined which contain the Nogana trypanosome or spirochete of recurrent fever there have been found large deposits of arsenic after salvarsan treatment, while in all of the examinations of control subjects not containing spirilla no trace of arsenic could be found. These researches are strictly in accord with the supposition of the parasitotropic action of salvarsan. K. Ullmann (Wiener klin. Woch., Feb. 6, 1913).

The minimal concentration of chemicals required to kill *Trepomena pallidum* of a heavy type was, of mercury bichloride, 1 to 200,000; arsenic trioxide, 1 to 30,000; tricresol, 1 to 500; salvarsan, 1 to 1000; neosalvarsan, about the same as salvarsan. Minute quantities of the antiseptics, far below the sterilizing point, were found to stimulate markedly the growth of spirochetes. The toxic effects of salvarsan were found to be increased from two to five times in the presence of liver and especially blood enzymes. J. Bronfenbrenner and H. Noguchi (Jour. of Pharmacol. and Exper. Therap., March, 1913).

In addition to its parasiticidal effect, salvarsan appears to improve directly the general nutrition of the body, after the manner of small doses of inorganic arsenic.

Effect on the Wassermann Reaction.—Salvarsan changes a positive Wassermann reaction into a negative one with greater ease than mercury. Upon repeated injections of the drug, a negative reaction will generally be noted in a month to six weeks, especially in early cases. The more efficient and prompt the antisyphilitic treatment, whether arsenical or mercurial, has been, the sooner will the positive reaction disappear. The latter event is by no means, however, to be construed as an indication to stop treatment, for the negative Wassermann does not show that the disease has already been eradicated, but only that it has been changed from an active state to one of inactivity for the time being.

The best results as regards the disappearance of the complement fixation test and the occurrence of relapses are obtained in the treatment of patients in the primary stage of lues, and the poorest in the treatment of those in the tertiary stage.

The reaction disappears somewhat more rapidly, however, in the tertiary stage than in either the primary or secondary stage of the disease.

The reaction disappeared during the second, third, and fourth weeks after treatment in the vast majority of the negative cases. The reaction disappears more rapidly after intravenous administration of salvarsan than after intramuscular. Craig (Archives of Intern. Med., Sept. 15, 1911).

Report of results of Wassermann test in 85 cases of **syphilis** in secondary stage treated with salvarsan. The test was negative in from four to eight weeks after the injections in the majority of cases, but in more than half of these the reaction became positive again from three to twelve months later. In some cases the disease ran a malignant course with a constantly negative Wassermann reaction. In 1 malignant case, mercury having proved ineffectual, under salvarsan the manifestations of the syphilis temporarily subsided, while at the same time the previously constantly negative Wassermann findings became positive. Salvarsan does not seem to insure a permanent cure. Müller (Wiener klin Woch., Bd. xxv, S. 873, 1912).

Observations on the value of the Wassermann reaction as a guide to the treatment of **syphilis.** In the primary stage, when the reaction is negative before treatment is commenced, most cases give a positive reaction afterward. This reaction is most marked about the forty-eighth hour, though in some cases it does not become positive until the fifth day. The degree diminishes generally about the third week, until it becomes negative before the eighth week. If the first injection gives rise to only a weak reaction, then three or four more will undoubtedly suffice to make the reaction permanently negative; if, however, the reaction is strong, the patient is in the secondary stage, and will require at least 3 Gm. of salvarsan or neosalvarsan. In the secondary stage, when the reaction becomes strongly positive after an injection, and in cases in which it is markedly positive before treatment, no blood tests need be made until before and after the fourth injection, as four injections are the minimum likely to be required to produce a permanent negative result. In the tertiary stage the Wassermann reaction behaves much in the same way as in the primary and secondary, except that a case with a strong positive reaction before treatment may become negative immediately after an injection and remain so from twenty-four to seventy-two hours, and then become positive again. Patients who have had syphilis and give a negative Wassermann reaction are either cured or in the latent stage, which of the two can only be ascertained by giving a provocative injection of salvarsan and then testing the blood. As an injection of salvarsan will not give rise to a positive reaction in a non-syphilitic, one must regard the occurrence of such as indicative of the presence of disease, and efforts should be made to bring about a cure. Three to seven injections are necessary to cure most cases of syphilis. Many cases in the tertiary stage can be cured with neosalvarsan which failed to be cured with salvarsan. The alterations in the Wassermann reaction as the result of treatment are most constant, and when tested at short intervals give a much safer guide to regulate treatment than by saying that just so many injections will be required. Patients should have a provocative injection of neosalvarsan six months or a year after they have been discharged, and the blood be tested forty-eight hours, the seventh, fourteenth, twenty-first, and twenty-eighth day after that injection. McDonagh (Brit. Med. Jour., June 8, 1912).

Salvarsan given to 472 syphilitics. The so-called provocative effect of salvarsan, *i.e.,* a negative Wassermann reaction becoming positive after the injection, or, if already positive, becoming more marked, was noted in 12 cases, of which 8 were tertiary syphilis, 1 locomotor ataxia, and 3 secondary syphilis. One case showed obstinate persistence of positive Wassermann reaction. Millard (Austral. Med. Gaz., Aug. 3, 1912).

In controlling the treatment by the Wassermann reaction it must be borne in mind that from 10 to 15 per cent. of the active late manifestations of syphilis give a negative reaction, so that, in the face of positive clinical findings and a negative test, the latter may be disregarded in the late stages of the disease. The author has on several occasions administered salvarsan to patients with a negative Wassermann with the very best results. In 1 case with a marked onychia involving the nails of the hands and feet, a decided change took place after the second injection. John A. Fordyce (Jour. Amer. Med. Assoc., Oct. 5, 1912).

The writer has steadily limited the initial dose to 0.6 Gm. for salvarsan and 0.9 Gm. for neosalvarsan, not repeating the same under thirty to sixty days. For a time he pushed the treatment beyond the ordinary clinical and Wassermann requirements, but his results confirmed the impressions obtained from previous experience, namely, that clinical and laboratory relapses were not thereby more favorably circumvented, and that persistently positive Wassermanns could not be materially changed by such a procedure. If one or two salvarsan administrations failed to effect the desired result, a dozen closely repeated would not change the situation, even if they were otherwise well tolerated. M. L. Heidingsfeld (Lancet-Clinic, March 22, 1913).

In cases where the reaction has been negative for some time a "provocative" injection of salvarsan will nearly always cause a return of the positive reaction in cases where the disease has not been definitely removed. This change takes place usually very promptly, the degree of reaction being generally most marked within twenty-four hours after the injection. It does not persist long, however, nearly disappearing by the fifth day in most instances (Gennerich, McDonagh). In the opinion of many observers these provocative injections constitute the most reliable means at hand to determine just when syphilis has been overcome and treatment is no longer necessary. According to Gennerich, however, the negative result of such a test is not to be absolutely accepted as a proof of the eradication of the disease until at least eight months have elapsed since treatment has been discontinued.

The best mode of treatment is as follows: An intensive initial cure, either with salvarsan alone or salvarsan combined with mercury. The Wassermann reaction must be carefully watched for six to eight months. If it remains negative, a "provoked Wassermann" should be tried, and repeated after a further six to eight months. Thus we are able to recognize complete cures in the course of one to two years, or to recognize possible recurrences in their earliest stages and to definitely cure them by repeated injections. P. Ehrlich (Münch. med. Woch., Nov. 21, 1911).

Mercurial and salvarsan injections are given by the author until a negative Wassermann is obtained in the blood tested twenty-four hours, the fifth and the fourteenth day after the last injection. Twelve months later he gives a provocative injection. It is possible that this last injection is superfluous, but in the present imperfect state of our knowledge it is wise to be cautious. J. E. R. McDonagh ("Salvarsan in Syphilis and Allied Diseases," London, 1912).

Indications for Salvarsan Treatment in Acquired Syphilis.—Though at first brought out by Ehrlich as an independently curative remedy for syphilis, salvarsan has, on the whole, proven itself more valuable for combined treatment with mercury.

Value of salvarsan in meeting the following indications emphasized: Prompt removal of severe genital lesions. The prevention or prompt removal of disfiguring skin lesions. In precocious or malignant **syphilis** and obstinate destructive bone and cartilage lesions, especially of the face and nose. Cases resistant to or intolerant of mercury. Early nerve and brain and all visceral lesions, with the exception of renal syphilis, in which salvarsan is dangerous. In late lesions of the nervous system its use may occasionally be justifiable. Cases of syphilitic cachexia or anemia, which often consist of a combination of overtreatment and syphilis. Severe and rapidly destructive lesions of the throat and obstinate lesions of the tongue. Syphilis involving the organs of special sense, excepting lesions involving the retina. Early **tabes** or, exceptionally, late—not terminal—cases, in the hope of relieving severe pain or involvement of the sphincters. Infantile syphilis. G. F. Lydston (N. Y. Med. Jour., Oct. 21, 1911).

Salvarsan is especially indicated as follows: (1) In very early cases, upon the very first appearance of the **chancre**, excise the chancre and administer salvarsan at once, thus aborting the disease. (2) In recent cases, in which rapidity is desired to clear up as soon as possible the skin lesions or mucous patches; these cases to be followed up with mercury. (3) In cases in which tuberculosis is developing upon a syphilitic base. (4) In cases of great anemia which might be aggravated by the further use of mercury. (5) In old tertiary cases, and rare cases in which mercury and potassium iodide singly or combined had been consistently and persistently used for a long period of time without results. In all cases, whether treated by mercury or salvarsan, the treatment should be guided by frequent Wassermanns. Woodward (St. Paul Med. Jour., July, 1912).

Special indications for salvarsan enumerated as follows: (1) As an abortive treatment combined with excision of the chancre when possible, and followed by an energetic course of mercurial treatment. (2) All cases of **syphilis** with manifest symptoms. (3) Latent syphilis with a positive Wassermann reaction. (4) Doubtful cases of **tabes** and **general paralysis.** (5) In cases where there is an idiosyncrasy against mercury and patients are too easily salivated. (6) Where mercury has had but little effect in healing lesions or when relapses take place rapidly after using. (7) In cases when, after considerable mercurial treatment, the Wassermann reaction still remains positive. (8) Malignant syphilis. (9) **Gummata** of vital organs. (10) Painful **periostitis.** (11) **Congenital syphilis.** H. H. Morton (Genitourinary Dis. and Syphilis, p. 551, 1912).

It is necessary to administer salvarsan in courses of intravenous injections. Such courses should consist of five or six injections at intervals of from five to seven days. The treatment of secondary syphilis with one or two injections without further treatment cannot be too strongly condemned. Such treatment alters the body reactions so that relapses are at times more severe than in patients poorly treated with mercury. In addition, the patient has a false sense of security and wastes much valuable time as well as the benefit of the treatment already received. It has been fairly well shown that a course of salvarsan is much more effective if preceded by a course of mercury intramuscularly or by inunctions. This preliminary mercury treatment also eliminates the probability of a febrile reaction, which so often follows the first intravenous injection of salvarsan in florid syphilis, and thus renders much safer the administration of salvarsan in dispensaries. H. P. Swift (N. Y. Med. Jour., May 17, 1913).

Primary Stage.—Since there is a distinct possibility that, if salvarsan is injected in the primary stage of the disease, the infection will be entirely overcome, and since conclusive laboratory methods of confirming a diagnosis of syphilitic chancre are now available, the course formerly recommended, viz., waiting for secondaries to appear before beginning treatment, is no longer justified. In cases where the surgeon is not convinced from the appearance of the lesion that it is syphilitic, little or no difficulty will be experienced in examining scrapings from the sore by the India ink, "dark ground," or other methods for the detection of the organism—*Spirochæta pallida*. Where doubt is occasioned owing to the presence of a double chancroidal and syphilitic infection, it will soon be dispelled through the fact that the lesion will not heal, or will improve only temporarily, under the usual treatment for chancroid. Upon continued observation—until the incubation period of the chancre has expired—further local disturbance will be observed.

For the reasons above mentioned, an injection of salvarsan (or neosalvarsan) should be given at the earliest opportunity in primary syphilis. In a few days the sore will have healed. The Wassermann test should be tried two days after the injection and, if the test is positive at that time, further treatment should be given, viz., another injection of salvarsan after a suitable interval, followed by mercurial treatment—preferably by inunction. Intravenous injections are much more rapid in their action on the chancre and in causing the spirochetes to disappear than intramuscular injections; hence they should be given the preference. Some observers lay stress on excision, cauterization or mercurial inunctions of the chancre as necessary measures in incipient syphilis.

While salvarsan is beneficial in the majority of cases, a single injection frequently fails. Preliminary or conjoint treatment with iodine and mercury renders the treatment with salvarsan more satisfactory. Sarkisoff (Roussky Vratch, June 16, 1912).

Of the primary and secondary cases among 350 **syphilitics**, not one failed to clear within a month after salvarsan; nearly all in a week to ten days. A little pigmentation was not infrequently left, but this cleared gradually without further treatment. In no primary case did a secondary rash develop. Tertiary cases, including huge ulcerations with splinters of dead bone at the base, and measuring in one case over two inches across, cleared, granulated, and healed as fast as epithelium could grow over. Congenital cases are more obstinate, especially **interstitial keratitis,** but even this certainly improves. **Tabes,** except in the late stage, seems greatly to benefit. Not one lesion in the 350 cases resisted more than three injections, though among them were numerous patients treated for a long time, thoroughly but unsuccessfully, with mercury. There were about 20 recurrences, all treated early with small doses, intravenous or intramuscular, and 2 only with three injections given intravenously; in each of these latter cases the dose given was 0.4 Gm. or under. Among private patients, none of whom received less than three injections, some 4 or 5, and of whom only one-half received any mercury, none recurred. Since following the practice in hospital of giving injections until the Wassermann became completely negative, no case has recurred, although only a very small number have received mercury afterward. Molesworth (Austral. Med. Gaz., Aug. 3, 1912).

In the early period it may be possible with one, two, or three doses to eradicate the infection. During the secondary stage it is more difficult, and in the still older ones still more of the drug must be used. The initial dose for men should not exceed 0.4 Gm. and 0.3 Gm. for women, until the susceptibility has been tested. In the early stage three or four doses, supplemented by mercury, will in many cases cure the disease in from six months to a year. The florid stage requires more intensive treatment—five or six doses followed by several mercurial courses are necessary. J. A. Fordyce (Jour. Amer. Med. Assoc., Oct. 5, 1912).

In otherwise healthy people in the primary and early secondary stages of the disease, the average dose is 2 Gm., given in three portions with intervals of two to five days between, followed by a month of mercurial treatment, so conducted as to produce no deterioration in general well-being, and a final salvarsan injection of such size as previous experience has shown will be tolerated. If cerebrospinal symptoms be present, the mercuric treatment should precede the salvarsan. From a single injection, even a large one, little more than a symptomatic and temporary cure can be expected. Edward Martin (Penna. Med. Jour., Nov., 1912).

Thirty-five patients with primary **syphilis** treated at the period when the Wassermann reaction was still negative. Each received three salvarsan injections of 0.5 to 0.6 Gm. in men and 0.4 in women, the interval between injections being from fourteen days to three weeks. None exhibited secondary symptoms, and the Wassermann reactions remained negative. Two of these patients became reinfected. Krefting (Berl. klin. Woch., Nov. 4, 1912).

Abortive cures are more readily obtained with neosalvarsan and mercury than with mercury treatment alone. Untoward by-effects are usually only observed after the first injection of neosalvarsan. Therefore, it is advisable to begin the treatment, especially of cases of very active **syphilis,** with small doses. It is also necessary, to avoid unpleasant symptoms, that the intervals between doses should not be too short. Kerl (Wiener klin. Woch., Nov. 7, 1912).

In rare cases of syphilitic infection there may occur, simultaneously with the roseola, or even before it, symptoms of severe nephritis, such as very marked albuminuria and widespread edema. The symptoms may develop gradually or very rapidly. In the catheterized urine the spirochetes are found. The cure of the **syphilitic nephritis,** which may be superimposed upon an already impaired kidney and is characterized by a specific alteration of the glomeruli, is best accomplished by a carefully combined mercury-salvarsan treatment. E. Hoffmann (Deut. med. Woch., Feb. 20, 1913).

Secondary Stage.—In cases first seen in the secondary stage the same promptitude in administering salvarsan as in the primary stage is desirable, not only because the sooner the disease is taken the less subsequent trouble is likely to occur, but because the injection, by sterilizing the spirochetes, causes the patient to become non-infectious, thus protecting the community from further transmission of the disease. Although no definite plan of treatment has as yet been agreed upon by all, persistent salvarsan treatment, alternating with mercury, is conceded to be the most efficient procedure in secondary syphilis. Repeated intravenous injections of salvarsan or neosalvarsan should be given at intervals at first of one week, later of two or three weeks, until the Wassermann reaction, tested twenty-four hours, five days, and two weeks, respectively, after an injection, proves uniformly negative. Mercurial treatment should also be given (McDonagh), preferably by intramuscular injection or inunction.

Every patient with active infective lesions of **syphilis** should receive salvarsan. Patients with such lesions—eroded chancres, moist papules, condylomata, mucous patches—whose surfaces are swarming with spirochetes are a menace to their entourage and the community. A single dose of salvarsan will render such patients harmless within a few days, often within twenty-four hours. S. Pollitzer (N. Y. State Jour. of Med., June, 1911).

A single dose of salvarsan, as a rule, produces only a mild parasitotropic action; the good results following an initial dose may be due more to its organotropic effect, improving an existing anemia, and stimulating body metabolism. The author administers pilocarpine hydrochloride in doses of from 1/32 to 1/16 grain, well diluted, three times a day by mouth, or hypodermically, for two days before giving salvarsan, with the idea that it will stimulate the glandular system and also wake up latent spirochetes into activity, so that they may be more readily reached by the salvarsan. J. L. Boehm (N. Y. Med. Jour., Dec. 2, 1911).

In the secondary and tertiary stages of **syphilis** one or more intravenous injections, with a week's interval, should be given, until the symptoms are under control, and at the same time an intensive treatment with mercury be given for one month to six weeks. Then the entire procedure should be repeated, the amount of salvarsan to be given being gauged by the serum reaction. H. J. Nichols (Jour. Amer. Med. Assoc., March 2, 1912).

All cases of **lues** should complete their supposed cure with an intramuscular injection or injections, particularly in cases of more than three months' standing. Mercury should be used regularly in the treatment of **syphilis**, following up the salvarsan. In tertiary syphilis potassium iodide should also be used. Patterson (Military Surgeon, May, 1912).

When an early and effective calomel treatment is used, less salvarsan is necessary. A proper combination of the two drugs makes it possible to cure **syphilis** in one-sixth the time required when calomel alone is used; and the treatment is much milder. In secondary cases the author usually begins with a calomel treatment of eight intramuscular injections: two of 70, two of 60, two of 50, and two of 40 mgm. If the patient has serious secondary symptoms such as laryngeal syphilis with intense and constant cough and almost complete loss of voice, he is immediately given two or three intravenous injections of salvarsan, three or four days apart, before the calomel treatment is begun. The injections of calomel are given every four to five days, and if the patient's condition allows he receives two more injections of 40 mgm. each when the first eight are complete. During the calomel treatment the patient must take the very best care of himself; he should stop work if possible, must go to bed immediately after each injection, and must refrain from the use of alcohol for an indefinite period. The intravenous injections of salvarsan, which follow the calomel after a few days, quickly bring the patient back to a state of comparative well-being. The injections of salvarsan are made at intervals of from three to four days; and five or six injections are given in all. Men receive from 0.5 to 0.6 Gm. salvarsan at each treatment, while women are given somewhat less. The calomel must be given as a fine suspension in oil of sesame. W. F. Boos (Boston Med. and Surg. Jour., Sept. 19, 1912).

The efficiency of salvarsan bears a direct relation to the age of the infection. In the early stage three or four doses supplemented by mercury will in many cases cure the disease in from six months to a year. In the florid stage five or six doses followed by several mercurial courses are necessary. J. A. Fordyce (Jour. Amer. Med. Assoc., Oct. 5, 1912).

Treatment in the early secondary stage must be vigorous and prolonged. A radical cure must not be attempted with less than three or four intravenous injections of salvarsan, combined with an intensive treatment with mercury over a period of at least two months. It is of great advantage if an examination of the spinal fluid can be made, because an increased cell count and protein content indicate the cases which are potentially those of nervous relapse. H. J. Nichols and W. H. Hough (Jour. Amer. Med. Assoc., Jan. 11, 1913).

The skin and mucous membrane lesions of the secondary stage rapidly disappear under salvarsan. Macular eruptions begin to fade within twelve hours after an intravenous injection and a few days later are entirely gone. Mucous patches, condylomata, and secondary periostitis likewise often disappear in two or three days, —a much shorter period than is the case with mercurial treatment. Papular eruptions are not so promptly removed, especially when the individual lesions are of large size, and after they have been overcome pigmented spots may persist for some time at their sites. Pustular lesions show prompt improvement, however, especially if suitable local detergent and antiseptic treatment is simultaneously applied. Recurrent syphilides, including lichen syphiliticus, generally disappear more rapidly than the first, though the papular and squamous forms may still prove obstinate. Other manifestations of secondary syphilis, such as joint and bone pains, nocturnal headache, and alopecia come to an abrupt standstill when salvarsan is given.

Case in which after intramuscular injection of 0.6 Gm. of salvarsan the symptoms of syphilis—chancre (spirochetæ positive), Wassermann ++, lymphadenitis, papulopustular eruption—disappeared. After the treatment the Wassermann reaction was —, and the patient was discharged without symptoms. A year later, while the Wassermann reaction was still negative, he reappeared with a chancre, lymphadenitis, and a characteristic maculopapular exanthem. Then the reaction that had been negative became positive. The case seems to be one of true reinfection with syphilis after treatment with salvarsan. Klausner (Münch. med. Woch., Oct. 31, 1911).

A patient excreted 5.4 per cent. glucose without acetone. He lost considerable weight, his stools were fatty and contained undigested meat, and a tender induration could be felt in the region of the pancreas. The Wassermann reaction being decidedly positive, 0.4 Gm. of salvarsan was injected. The effect was almost immediate. The induration disappeared and no sugar could be found in the urine, though the patient was on a mixed diet. He steadily gained in weight, and a year after the injection was apparently in perfect health. Many cases of **acute yellow atrophy of the liver** are syphilitic in origin and are amenable to salvarsan. In 1 case there were all the typical symptoms; the urine contained many crystals of leucin and tyrosin and the liver appreciably decreased in size within twenty-four hours. An intravenous injection of salvarsan, 0.4 Gm., checked the process at once, and the patient rapidly recovered from an affection which otherwise would have been surely fatal. Umber (Münch. med. Woch., Nov. 21, 1911).

One patient with very large, flat, papular **syphilide** was not cured after four intravenous injections of "606," nor was much improvement obtained by previous and subsequent application of mercury. Ballenger and Elder (Med. Record, Dec. 2, 1911).

The author made 516 injections of salvarsan in 395 patients, of whom 382 were syphilitic. The majority of the injections (396) were made intravenously. With the exception of 37 recurrences, the results were very satisfactory. In 2 cases of syphilis complicated, 1 by a grave nephritis and the other by diabetes, repeated injections of fractional doses of salvarsan were not followed by any reaction. Neither the nephritis nor the diabetes was benefited. Two patients with **relapsing fever** recovered, the spirochetes disappearing eight hours after the injection. In 1 case of tuberculosis of the throat and in 2 cases of cerebral tumors the results were negative. Galpern (Roussky Vratch, June 16, 1912).

Intense **headaches,** often so persistent during the secondary and tertiary stage of the disease and due to a low-grade meningitis, usually remit with remarkable rapidity under salvarsan. J. A. Fordyce (Jour. Amer. Med. Assoc., Oct. 5, 1912).

Especially remarkable are the results obtained in the "malignant" forms of syphilis in which mercury has failed and the patient is suffering from anemia, severe ulcerations of the mucous membranes, and gummata of the skin. Cases of syphilis complicated with tuberculosis of the lungs have been reported in which salvarsan produced an excellent effect on both diseases.

Cases of **syphilis** complicated by **pulmonary tuberculosis** should receive salvarsan, which is not only of value in improving the syphilis, but actually by its good effect on metabolism benefits the tuberculosis. Where cavities are present in the lungs intramuscular rather than intravenous injections should be employed. S. Pollitzer (N. Y. State Jour. of Med., June, 1911).

Tertiary Stage.—In this stage salvarsan will not only cause most gummatous lesions to disappear with surprising rapidity, but will accomplish this where mercury and potassium iodide have alike failed, and, furthermore, will tend to prevent their recurrence. In a few instances, however, healing will not take place until accessory measures, such as local antiseptics and the internal administration of the iodide, are combined with the salvarsan. The scars left by gummata that have healed under this drug are far less conspicuous and adherent and more supple than those remaining after other treatment.

Historical studies of various skin lesions of **syphilis** under the influence of treatment, particularly with salvarsan. The specific infiltrations persist for some time, though the diffuse leucocytic infiltrations disappear more rapidly. The early institution of treatment and the administration of salvarsan at frequent intervals markedly influence the quality and rapidity of disappearance of the infiltrations. Endarteritic changes are strikingly affected by treatment. Following salvarsan, the elastic fibers undergo further injury, and may disappear entirely; in other words, elastic tissue is less affected by the living spirochetes than by their endotoxins. Rohrbach (Münch. med. Woch., Bd. lix, S. 967, 1912).

Salvarsan also causes a remarkable improvement in the patient's general state, bringing about an increase in the body weight, a subjective feeling of marked physical and mental betterment, increased appetite, and relief from such complaints as headache, giddiness, precordial pain or oppression and palpitations (McDonagh). As in the secondary stage, obstinate ulcerations of the pharynx and larynx, causing dysphagia and sometimes pronounced stenosis of the respiratory passages, can be promptly relieved with the remedy. Such uncommon but troublesome manifestations as serpiginous syphilides, chronic glossitis, Ménière's syndrome, pulmonary syphilis, and syphilitic arthritis can be more or less rapidly overcome by intravenous injections of salvarsan.

> In the tertiary stage the infecting cause is not readily attacked, as the lesions are in the deeper, firmer structures. Large doses of salvarsan are not indicated, except in very rapidly progressive and destructive lesions. It should rather be given so as to be effective constantly, *i.e.*, the dosage should be small, 0.3 Gm. given once a week, or once in two weeks. As salvarsan has no action in breaking down pathological tissue, it is necessary to give the iodides, which should be administered in increasing dosage except in laryngeal conditions in which much narrowing of the lumen is present.
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> When the patient appears cured, the iodides should not be discontinued but given regularly, whereas salvarsan should now be given every six or eight weeks in the dose of 0.3 Gm. for several doses. Then all medication should cease and blood examinations be carried out every five or six weeks for several months. F. W. White (Laryngoscope, Sept., 1912).

According to McDonagh any case of tertiary syphilis can be cured if the treatment is carried out with sufficient energy and persistence,—at least a permanently negative Wassermann reaction can be secured. In tertiary cases where there are no symptoms but the Wassermann is positive, salvarsan is hardly necessary; for if symptoms appear at any time, they can be quickly eradicated with the drug. In patients coming under observation with definite tertiary symptoms, however, salvarsan, mercury, and potassium iodide may be used simultaneously.

To render the Wassermann constantly negative in these cases, about 3 Gm. of salvarsan will, in general, be required.

> A good treatment with salvarsan is always necessary to avoid neurorecurrence. The combined treatment with calomel and salvarsan is able to cure any case of syphilis. The average dose needed is about 2½ Gm. In the provocative injection of salvarsan we have an apparently trustworthy method by means of which to distinguish between latency and cure after treatment has been discontinued for perhaps a year. Very rarely, in old tertiary cases, there is a positive fluctuation only after a second injection. Gennerich (Berl. klin. Woch., Oct. 2, 1911).
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> Report of a case of chancre making its appearance four days after an intravenous injection of salvarsan in an old case of syphilis. The Wassermann test had been negative for years, but symptoms of locomotor ataxia had appeared. The examination of the serum from the sore showed undoubted spirochetes and the Wassermann was positive. M. Rosenthal (Jour. Amer. Med. Assoc., Dec. 21, 1912).
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> Salvarsan acts favorably in the third stage and in **hereditary lues,** less favorably in the secondary stages; in the latter the administration of small, gradually increasing doses is especially to be recommended. O. Kren (Wiener klin. Woch., Jan. 23, 1913).
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> Salvarsan effects an apparent clinical and laboratory cure in about 75 per cent. of the cases treated. A very large proportion of the remaining 25 per cent. of cases, with the aid of mercurials, cacodylate of sodium and other measures, give every promise of proceeding to a negative Wassermann and clinically absolute cure in

due course of time. M. L. Heidingsfeld (Lancet-Clinic, March 22, 1913).

Lesions of the Organs of Special Sense.—Although the occasional apparent untoward effects of salvarsan on certain of the cranial nerves at first tended to discount its value in syphilis of the special sense organs, more recent experience has fairly definitely shown the drug to be equally as useful in involvements of this nature as in overcoming the superficial—skin and mucous membrane—manifestations of the disease. Such serious phenomena as **iritis, iridocyclitis, interstitial keratitis, optic neuritis, neuroretinitis, chronic otitis media** and **deafness, aphonia, syphilitic nasal catarrh,** and progressive **deformities** of the **nose** and **palate,** alike yield more or less rapidly to the new drug.

Many of the so-called bad results of injections of "606" are similar to the lesions which one might quite easily find in the ordinary course of syphilitic infections. The best results from its use were obtained in cases of iritis, but lasting good resulted in 1 case of typical **heredosyphilitic keratitis.** F. de Lapersonne and André Léri (Arch. d'ophtal., Jan., 1911).

Salvarsan is very effective in secondary and tertiary manifestations of the uveal tract. It causes no appreciable subjective or objective symptoms on the healthy eyes of syphilitics. Rosenbaum (Med. Rec., July 22, 1911).

Eye cases classified into three groups: those in which good results are produced, those in which the result is doubtful, and those in which the effect of salvarsan is neutral. To the first group belong **iritis** and **iridocyclitis,** as well as probably descending **optic neuritis** and **atrophy.** Doubtful cases are those of choked disk and certain cases of ascending neuritis. No benefit can be expected in opacities of the vitreous, or in old miosis and mydriasis. Dolganoff (Berl. klin. Woch., Nov. 6, 1911).

A patient presented a gummatous ulceration of the external nose with necrosis of the septum and specific ear trouble. He was in very poor physical condition, could not tolerate even mild mercurial treatment, and in addition had aortic insufficiency owing to previous rheumatism. The use of salvarsan in the customary doses seemed out of the question. The author therefore gave only 0.05 Gm. in neutral suspension into the muscles. Within several hours a local reaction appeared about the ulcers, with increased secretion. After twenty-four hours the reaction had disappeared and in two days the specific process began to heal. The injections were repeated every third or fourth day, and after fourteen days (four injections = 0.2 Gm. salvarsan) all ulcers were closed. Three more injections were given, which greatly improved the general condition. Hearing was restored to normal, but the valvular lesion was not influenced. It is probable that salvarsan in such small doses may be used to advantage in many cases where it is ordinarily contraindicated. L. Waeloch (Münch. med. Woch., Nov. 21, 1911).

The author has given salvarsan, with rapid and marked benefit, in several cases of **retinochorioiditis** with sudden blindness. When the optic nerves are diseased, even in an advanced stage, and in emergency conditions, he does not fear to administer salvarsan; but he gives it only intravenously, as all the cases of involvement of the cranial nerves following the use of salvarsan have occurred where the drug had been used intramuscularly. Neuritis of cranial nerves after salvarsan is merely coincidental and only a syphilitic inflammation of the nerve proper without connection with the arsenic. Yet it is a wise precautionary measure to have an ophthalmoscopic examination made preceding the intravenous use of salvarsan. J. L. Boehm (N. Y. Med. Jour., Dec. 2, 1911).

Report of 2 cases of **acute iritis** with condyloma, in which there were rapid subsidence of the inflammatory symptoms and disappearance of the condyloma following injection of salvarsan. The treatment caused entire disappearance of the inflammatory symptoms in eleven days in a case of chronic general **uveitis.** In a case of a low form of long-continued general **uveitis,** there was no immediate result. In 4 out of 5 cases of **interstitial keratitis** treated, there was a rapid disappearance of circumcorneal injection, photophobia, and lachrymation. In 3 cases there was no exceptional rapidity in the clearing of the corneal infiltration. F. E. Cheney (Boston Med. and Surg. Jour., Dec. 21, 1911).

Salvarsan is of value in **syphilis of** the **ear,** especially in recent aural lues. In old aural lues its use should be guarded, especially if there is degeneration of the cochlear or vestibular nerves. If it is injected while the child is young, it may be useful in congenital deaf-dumbness. Voorhees (Amer. Med., July, 1912).

Syphilitic lesions in the **throat** healed with remarkable rapidity under salvarsan, although most of them had resisted treatment by the older methods. Laryngeal syphilis has shown less marked improvement, owing perhaps to ulceration, scar tissue, ankylosis of the arytenoids, etc. F. C. Cobb (Laryngoscope, Sept., 1912).

Laryngeal cases with marked stenosis should be treated in hospitals and the iodides either not administered at all or only when definite increase in the size of the lumen of the larynx is demonstrable. These cases may suddenly develop edema of the larynx when receiving the iodides. F. W. White (Laryngoscope, Sept., 1912).

Three pronounced cases of **interstitial keratitis** treated by salvarsan, which was introduced in an oil vehicle intramuscularly. The drug acted so quickly that little connective tissue had time to form. In each case the corneal infiltrate was absorbed to a much greater degree than could be hoped for with mercury. One does not expect to absorb the old scars of a past interstitial keratitis with salvarsan, but if the drug is used when the least trace of acute symptoms is present it will check inflammation, absorb infiltrate, and prevent further deposit. Vandegrift (Med. Record, Oct. 26, 1912).

Neosalvarsan preferred for affections of the anterior parts of the eye, and salvarsan for affections of the retina and optic nerve, especially when the nervous system is attacked in any way. J. Igersheimer (Ophthalmoscope, Nov., 1912).

Occasionally resistant ulcerations (particularly those of the pharynx) are met which improve up to a certain point, and then cease to improve under salvarsan only to yield to vaccine treatment. Sometimes a case with well-marked polymorphic rash is seen, and the entire eruption is looked on as syphilitic. Salvarsan is given, and after one or two injections almost the whole rash is gone, but patches of eczema or some other type of rash are left. L. Kilroy (Lancet, Feb. 1, 1913).

The so-called *"neurorecurrences,"* consisting usually of lesions of the auditory and optic nerves appearing after a single injection of salvarsan, and which have been the subject of much discussion, are no longer considered due directly to the action of the drug—as was the case with atoxyl and arsacetin—but to a temporary accentuation by the drug of syphilitic nerve-lesions previously present. Only in 1 case—that of Finger—in a series of 30,000 patients with previously healthy eyes, treated with salvarsan, did Ehrlich find optic atrophy. In this instance the patient had received previous treatment with the other arsenicals; hence it is recommended not to use salvarsan where atoxyl or related compounds have already been administered.

The "neurorecurrences" appear especially in early syphilis, and rather constantly within a period of several weeks after the injection. It is generally recognized—notwithstanding the fact that greater care in the observation of the cases is now customary than formerly, and some cases are now recorded which would most likely have been missed in earlier years—that these "relapses" do occur after salvarsan oftener than otherwise, and must in some way, at least in a certain proportion of cases, be referable to the drug. Where the cochlear nerve alone is involved, deafness, either rapid or gradual, is complained of, while if the vestibular nerve is at fault there occur dizziness, tinnitus aurium, nystagmus, and vomiting. The ocular complications lead to headache, photophobia, conjunctivitis, and dimness of vision. Other cranial nerves sometimes involved are the facial, oculomotor, trochlear, abducens, and trigeminal.

> Inflammation of the optic, auditory, facial, and other cranial nerves has developed in a minute percentage of cases after the use of salvarsan in syphilis. The same complications may occur spontaneously or after the use of mercury. A risk is incurred in discontinuing antisyphilitic treatment for a long period in early syphilis, after a single injection of salvarsan, particularly when given subcutaneously or intramuscularly. Schamberg (Jour. Amer. Med. Assoc., May 20, 1911).
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> Case showing that among all the cranial nerves the eighth is the most easily affected by salvarsan. Disturbances in the optic, oculomotor, trigeminal, facial, acoustic, glossopharyngeal, and hypoglossal all occurred. After a number of months the functions of all the nerves became normal, with the exception of that of the eighth nerve, which remained permanently injured. Levinstein (Med. Klinik, July 14, 1912).
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> Salvarsan has a favorable effect on the secondary aural affection in that it eliminates the primary focus of the disease, *e.g.,* the plaques in the throat, and is therefore preferable to mercury in certain cases. Wherever the internal ear is normal, there are no otic contraindications to salvarsan.
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> Affections of the cochlear apparatus appearing simultaneously with cutaneous symptoms present no contraindications to salvarsan, for they are to be regarded as partial symptoms of the general luetic infection. The same applies where affection of the cochlear nerve is associated with middle-ear disturbances (mostly catarrhal).
>
> It is almost pathognomonic that ear affections appearing independently of cutaneous symptoms occur four to eight weeks after the injection of the salvarsan. A second dose of salvarsan is contraindicated in such cases of nerve affection. The safest therapy is a strong mercurial treatment.
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> In otosclerosis the nerve-elements of the ear are involved in the pathological processes and salvarsan is contraindicated. In 2 cases the hearing, according to the patients, grew rapidly worse after salvarsan.
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> Whether salvarsan is indicated in hereditary luetic deafness is still an open question, for, on the one hand, considerable improvement in the functional activity of the ear has been noted, and, on the other, an equally marked deterioration. Oscar Beck (Laryngoscope, Sept., 1912).

That these disturbances are not due directly to the drug is indicated by the fact that they are usually improved or entirely overcome by further injections of salvarsan or by mercurial treatment. Roscher advises the routine administration of mercury before the former drug is given at all, in secondary stage cases with well-developed lesions, while McDonagh states that since making it a rule to repeat salvarsan within an interval of a few days, and to combine it with mercury, he has had no more cases of cranial neuritis.

Cases of permanent involvement of the auditory, ocular, and other cranial nerves, even where salvarsan had been repeated, have been met with, but their number is small in comparison with that of cases similarly afflicted which have not been treated with salvarsan (Carpenter).

> The partial non-success of salvarsan in lues is due not to the drug, but to the disease—foci hard to penetrate or reach, local reactions due to setting free of the endotoxins. Improvements are not to be sought in a new drug, but in improved modes of application of the present one. P. Ehrlich (Münch. med. Woch., Nov. 21, 1911).

> There can be no injury to the nerve-elements of the eye by salvarsan, and the hyperemia of the nerve-sheath of the optic nerve, retinal hemorrhages, or central scotoma after salvarsan injections are merely the neurorecurrences of Ehrlich. Gebb (Med. Klinik, Sept. 1, 1912).

> Aural symptoms non-specific in origin do not contraindicate the administration of salvarsan, and if they are caused by some process specific in nature they furnish a positive indication for it. The contention of some that the remedy is not to be given in mild degrees of impairment of hearing or in unilateral deafness on the ground that it is liable to destroy the remaining hearing power is not supported by the facts. C. E. Perkins (Laryngoscope, Sept., 1912).

> Report of a case illustrating the fact that liberal injection of salicylate of mercury does not ward off paresis of an eye muscle and demonstrating the utter uselessness of salvarsan treatment unless subsequent blood tests are made to ascertain whether or not the patient is free from the disease. N. L. Wilson (Laryngoscope, Sept., 1912).

The immediate cause of the neurorecurrences, which are generally unilateral, appears to be usually an inflammation of the trunks of the cranial nerves concerned. The consequent enlargement is believed to bring about pressure upon the nerves at points where the surrounding tissues —as in bony canals—are unyielding, functional paresis or paralysis being the result. The inflammation itself, in turn, is probably due to the activity of spirochetes locked up in the nerves and not killed—but perhaps, on the contrary, stimulated—by the first injection of salvarsan. That the Wassermann reaction in these cases is negative seems due to the fact that the organisms locally present are not numerous enough to bring about antibody formation and itself also tends to substantiate the assumption that these organisms are in a sequestrated and sheltered situation where it is difficult for the salvarsan to reach them in sufficient amount.

> Early neurorecurrences are due to acute edema resulting from rapid death of spirochetal foci (particularly in nerves running through a rigid canal, like the auditory nerve), and can be compared to the erythematous skin eruptions noted where drugs are given. In a large series of cases observed, 194 early neurorecidives occurred after salvarsan injection, and 123 after mercury injections,—no very great disproportion. Late recurrences in the nervous system are due

to the fact that all but a few spirochetes, at some site not readily reached by the arsenic, have been killed, and that these organisms then have the oportunity to grow unhindered with greatly increased rapidity. Such nervous recurrences take place almost exclusively in the early secondary period, when there are most spirochetes in the body. That the arsenic is not at fault is shown in that they do not take place in the early stages of syphilis; that the nervous symptoms are cured by salvarsan; that in other spirilloses (frambesia, recurrent fever, etc.) no toxic symptoms ever arise. P. Ehrlich (Münch. med. Woch., Nov. 21, 1911).

Neurorecidives after salvarsan treatment vary markedly in the different clinics and seem to be particularly conspicuous in certain quarters. This gives rise to the suspicion that Ehrlich's injection rules are not followed scrupulously. When the solution is not injected immediately after its preparation, or when the solution during its preparation is stirred too vigorously, oxidation products are formed, much more poisonous than salvarsan, which probably have an affinity for the central nervous system. Cronquist (Münch. med. Woch., Nov. 12, 1912).

Syphilis of the Nervous System.—In nervous conditions dependent on syphilis the efficacy of salvarsan depends upon whether the condition present is merely one of inflammation with a possibility of complete resolution or has already led to destruction of nerve-cells. Among the first category are cases of **cerebral** or **cerebrospinal syphilis,** associated with a **cortical** or **basal syphilitic meningitis,** and manifested by headache, insomnia, irritability, psychic disturbances, dizziness, epileptic seizures, signs of involvement of cranial or spinal nerves, such as **ophthalmoplegia,** etc. These are the disturbances which generally occur within a few years after the infection and develop with considerable rapidity. In these the administration of salvarsan in doses not exceeding 0.3 Gm. will generally produce a notable and sometimes a most striking improvement. This drug should not be given, however, until after the stage of acute inflammation has passed, for a fatal ending, owing to primary aggravation of the process and pressure on intracranial centers, has been known to occur where this rule has been disregarded. Even at best, convulsive phenomena and temporary local paralyses may follow the administration of the drug. In recent cases of hemiplegia due to thrombosis, salvarsan should not be given, as there is danger of an excessive inflammatory reaction and of hemorrhage due to softening of the thrombus. Mercury inunctions should be used instead, and salvarsan not resorted to unless mercury loses its effect (McDonagh).

Case of severe **trigeminal neuralgia** in a woman who had never had any symptoms of syphilis, but whose serum gave a positive reaction, which was cured after an intramuscular injection of 0.5 Gm. in clear alkaline solution. Severe neuralgic pains in the legs in 2 syphilitics, twenty years after infection, disappeared after one intravenous injection of 0.4 Gm. in each case. Browning and McKenzie (Brit. Med. Jour., Sept. 23, 1911).

Seventy-five patients suffering from **syphilitic nervous disease** treated with salvarsan. The treatment is effective, but in order to get its best results large doses must be given and frequently repeated. Of 36 cases of **tabes** in various stages 22 showed striking and some remarkable improvement, both subjective and objective. In 2 cases the pupils regained their capacity to react to light. The results were incomparably better than those obtained by mercury. Salvarsan was given in 9 cases diagnosticated as **general paresis.** In 2 doubtful cases and 1 undoubted case of **paresis** great improvement took place. Gratifying response was observed in cases diagnosticated **meningitis** and **meningomyelitis.** In only 2 out of 6 cases of **cerebral endarteritis** of luetic origin was any perceptible improvement observed.

The average dose of salvarsan for an individual suffering from diseases of the central nervous system whose vitality is not conspicuously impaired is 0.6 Gm. In patients whose blood-pressure is high (above 165 mm. by the Stanton apparatus) and in whom there is very distinct evidence of cardiovascular degeneration, not more than one-half a dose should be given the first time. If the first administration is not followed within a fortnight by a chemical and microscopic evidence of cessation of activity of the syphilitic poison and the pathological process conditioned by it (negative Wassermann reaction, diminution of globulin, profound numerical reduction of lymphocytes in the cerebrospinal fluid), the dose should be repeated. The second dose should be the same as the first, unless some special reason exists for increasing or diminishing it. On the other hand, if the first dose is followed by indications of cessation of activity of the pathological process, the second dose should be delayed for from six weeks to three months.

One feature of salvarsan therapy of organic nervous diseases is the enormous physical uplift which many patients get, shown not only by a feeling of well-being and improvement, but by an increase of weight. Collins and Armour (Jour. Amer. Med. Assoc., June 22, 1912).

Excellent results obtained with salvarsan in 48 cases of various syphilitic affections of the central nervous system. In **lues cerebri** there was improvement or disappearance of facial paralysis and hemiplegia in 66 per cent. of the cases. Contractures disappear and convulsions are soon checked. Writing and general muscular power will approach the normal and pain and the paresthesia are alleviated. In 10 cases the psychic condition became normal and in 2 there was considerable improvement. In cerebrospinal lues, the gait was restored in 25 per cent. and there was decided improvement in the bladder and sexual functions. The general condition was usually influenced to a marked degree. In the initial stages of **tabes** the patellar reflexes may return and the ataxia, Romberg's symptom, gastric crises, lancinating pains and other pains may disappear entirely. In **dementia paralytica,** in the beginning stages, the pupillary reaction returned in 3 out of 28 cases and the tendon reflexes in 1 case. In 4 cases the gait was improved and in 11 cases the speech became more distinct. In a fair percentage, memory and the general intelligence returned, while in 3 cases the patients could again return to their vocation. Mercury and potassium iodide should be used in combination with the salvarsan, and in paretic dementia it is of advantage also to employ injections of sodium nucleinate. J. Donath (Münch. med. Woch., Oct. 22, 1912).

Lumbar puncture in 115 syphilitic patients showed that the pressure of the fluid and lymphocyte count present changes, sometimes very marked, in the preroseolic period and, especially, in the early secondary period. These correspond to a meningoencephalitis, and are sometimes accompanied by symptoms such as headache, vertigo, hyperacusia or hypoacusia, and evidences of paresis or paralysis of the oculomotor or facial nerves. From 7 cases, in each of which two or more lumbar punctures were practised, before and after repeated salvarsan injections, the author concludes that the nervous condition is probably favorably influenced by this remedy. The neurorecurrences are looked upon by the author as evidences of diffuse or localized syphilitic meningitis, rather than of the action of salvarsan. They can be cured or improved provided they are detected early, through close observation of the patient, including the cerebrospinal fluid, and combated promptly and persistently. Dind (Revue méd. de la Suisse Romande, March, 1913).

Neosalvarsan seems to have a milder and less intensive action than salvarsan. Therefore in inveterate **syphilitic diseases** of the **central nervous system** salvarsan is to be preferred. In most cases the combination of salvarsan and neosalvarsan has special advantages. G. L. Dreyfus (Münch. med. Woch., March 25, 1913).

Case of **brain syphilis** in which the condition of the patient seemed so desperate that in spite of the contraindication to the use of salvarsan in acute brain syphilis this treatment was resorted to. There followed rapid and complete recovery. N. B. Eddy (Jour. Amer. Med. Assoc. April 26, 1913).

In **tabes dorsalis** salvarsan is somewhat more than a palliative, though naturally incapable of causing regeneration of destroyed nerve-cells. It tends to relieve certain of the symptoms, but in many instances only temporarily. With repeated small doses of salvarsan more can be accomplished in this disease than with mercury and iodides. In cases with negative Wassermann reaction, however, its use is not advised. More marked results than in tabes are obtained in cases of cerebrospinal syphilis simulating the latter in their symptomatology.

The author has several cases of **tabes** and of **syphilis of the central nervous system** on record where a combination of salvarsan with mercury did more good than either drug alone. He has therefore made it a rule to use both drugs in these cases. O. L. Klieneberger (Berl. klin. Woch., March 4, 1912).

Salvarsan brings the **tabetic process** to a standstill. Furthermore, it can cause retrogression of certain lesions in the spinal roots or in the cord itself. The improvement is noticeable in the disappearance of the later symptoms and also, in some cases, of the older symptoms. The author observed a series of patients for two and half years, and in a few cases the patients were completely cured. The majority of the patients are now in a much better condition, the most prominent symptoms having almost altogether disappeared or showing marked attenuation. The dose is 0.01 Gm. (1/6 grain) of salvarsan or 0.015 Gm. (1/4 grain) of neosalvarsan to the kilo (2 1/5 pounds) of body weight. The treatment must be continued up to the entire disappearance of the positive seroreaction and every chronic and biological symptom which points to the fact that syphilis is still active. The effect of the drug upon the lightning pains is especially marked. The objective disturbances of sensation may also vanish completely. Gastric crises disappeared in all the cases treated. The ataxia was so improved that most patients could walk for long distances. The following symptoms were also favorably affected in a large number of cases: sexual impotency, bladder disturbances, headaches, bulbar symptoms, and laryngeal crises. New symptoms develop only exceptionally during the course of treatment if this is properly persisted in. Leredde (Münch. med. Woch., Sept. 24, 1912).

Salvarsan is indicated in **tabes** with a very positive serum reaction and a lymphocytosis of the cerebrospinal fluid; it should be given in repeated small doses at proper intervals. J. A. Fordyce (Jour. Amer. Med. Assoc., Oct. 5, 1912).

Where a syphilitic meningitis exists in **tabes** one can expect brilliant results from salvarsan as far as the symptoms due to the meningitis are concerned, and in early cases of tabes one can hope for a remission in the progressive course of the disease. A man, 45 years of age, with history of syphilis seventeen years previously, had complained of pains in the arms and limbs for some three months, more pronounced in the upper extremities. Reflex immobility of the pupils, vesical atony and girdle sensation were present, together with paresthesias and moderate analgesia and loss of deep-pressure pain sense in the lower extremities. Ataxia was absent, and the tendon reflexes were exaggerated. He had been impotent for some years. In this case the salvarsan cleared up the pains entirely, the exaggerated reflexes subsided, and the patient gained some twenty-five pounds in weight in the course of six months. The pupillary findings, analgesias, loss of deep pain sense, loss of the left Achilles reflex, and slowing of urination remain. The patient feels well and is engaged in business life. G. A. Young (Western Med. Rev., Feb., 1913).

While some slight improvement has followed the use of salvarsan in a few cases of **tabes**, the drug when pushed has intensified the destructive action of the disease and hastened the death of the patient. E. H. Trowbridge (Jour. Amer. Med. Assoc., Feb. 8, 1913).

Report of a case without syphilitic history, but giving a positive Wassermann reaction that showed the characteristic symptoms of **tabes**. It was first treated with mercurial inunctions and iodine; the patient was then given 0.6 Gm. of salvarsan, which was repeated some two and a half months later.

A month afterward, examination showed absence of the Argyll-Robertson pupil, improvement in the coordination, and less marked Romberg sign, together with gain in weight and a general feeling of well-being. J. J. Zaun (Jour. Amer. Med. Assoc., March 1, 1913).

Many patients with **syphilitic conditions of the cerebrospinal system** are aggravated by one or two doses of salvarsan, while, on the other hand, many of their symptoms are relieved by the persistent use of the drug. The pains, crises, bladder symptoms, and general nutrition are often greatly benefited. The author's plan of treatment in these cases is to give injections of salvarsan at weekly intervals, combining them with mercury at intervals of three or four days. In 1 case of paresis he gave twenty-one injections of salvarsan, about 10 Gm. in all, with marked alleviation of the symptoms. The Wassermann reaction in this case had not been influenced by the treatment. He is becoming more and more convinced that salvarsan has no deleterious effect on the optic nerve, having, on the contrary, 2 cases under observation where it proved distinctly beneficial. In 1 of these cases the visual fields have enlarged. J. A. Fordyce (Jour. Amer. Med. Assoc., May 17, 1913).

General paralysis is less amenable to salvarsan than tabes, though occasionally some symptomatic improvement is brought about. It is the consensus of opinion that the drug is of value only in the earliest stages of this disorder, and that its use in more advanced cases is attended with danger. In any event, only half a dose of salvarsan should be given, as in tabes and brain syphilis.

Case of a man, 40 years old, who began to suffer from dementia paretica; 0.5 Gm. of "606" was injected into the muscles beside the left scapula. For forty-eight hours he seemed to do well, then his temperature rose, his pupils became moderately contracted; then his feet and hands began to tremble, he could not stand, and he began to perspire freely. He lost his strength completely, though there was no paresis or edema and the tendon reflexes were lively. The heart and lungs showed no organic trouble, but he sank until death occurred. Autopsy revealed only a slight acute parenchymatous degeneration of some organs, particularly the kidney, and fatty degeneration of some fibers of the vagus and of the nerves in the right brachial plexus that could be ascribed to the poisoning with arsenic. The changes typical of dementia paretica were present in the brain. Jörgensen (Med. Klinik, March 5, 1911).

Fifty-six cases of **general paralysis of the insane** treated with salvarsan. In 12 patients there was a marked amelioration of symptoms; 6 of these were freed from restraint, and are pursuing their ordinary work. Browning and McKenzie (Brit. Med. Jour., Sept. 23, 1911).

Diagnostic Value of Salvarsan.—In obscure lesions in patients presenting no evidences or history of syphilis, salvarsan may be of considerable diagnostic value, its administration causing rapid improvement if syphilis is the cause.

In tertiary and latent cases of syphilis, with conditions present suggesting neoplasm, and with the Wassermann negative, a provocative injection of salvarsan, by causing the Wassermann to become positive if the disease is syphilitic, will in many instances prove of great assistance.

Salvarsan Treatment in Pregnant Syphilitic Women.—Such treatment has been found very advantageous, and unattended with danger, either of abortion or to the mother's life, provided moderate doses be used. The effect on the child depends upon whether the maternal syphilis was acquired before or during pregnancy as well as the time and number of salvarsan injections, etc. If the mother's infection is treated early the chances of her giving birth to a healthy child are good, whereas if salvarsan treatment is begun late in pregnancy, syphilis having been contracted some months before, the outlook is much less favorable.

Salvarsan cannot be given too early in pregnancy when symptoms of syphilitic disease are present. To prevent abortion and secure the birth of a healthy, non-specific child, the treatment should be followed by mercury and the Wassermann reaction used to note the result of the treatment. These observations reverse Colles's law, that mothers of specific children are immune if symptoms are absent. The serum test shows that such mothers are to be considered as infected. Langes (Wiener med. Klinik, Nu. 20, 1911).

A woman with secondary syphilis and in the sixth month of pregnancy was treated with 0.4 Gm. intravenously, repeated after five weeks. A healthy child was born at full time, and six months after the birth both mother and child were in good health. Browning and McKenzie (Brit. Med. Jour., Sept. 23, 1911).

Study of the effects of salvarsan administered intravenously in 10 pregnant women in doses of 0.5 Gm., and subcutaneously in 8 newborn infants in doses of 0.03 Gm. Injections of salvarsan in the dose mentioned are not without danger to the fetus, more probably owing to destruction of the treponemata than to a direct action. In about one-half the cases a pronounced weakening in the fetal heart sounds was noted in the days succeeding the injection, and in 2 cases there was some fear lest the child die in the three or four days after injection. The results yielded by the Wassermann test at a given moment in the mother and child may not correspond. Apparent maternal cure with negative serum reaction does not imply that the child is out of danger. The child of a mother in whom the first injection of salvarsan had been given five and one-half months before parturition was born healthy. A child born seventy-two days after salvarsan injection, however, was syphilitic. One woman developed grave albuminuria nineteen days after injection, and died five days after delivery, about five weeks after the injection, of pneumonia. Only 0.2 Gm. (3 grains) had better be used for pregnant women, repeated in six days. P. Bar (Bull. de l'Acad. de Méd., Oct. 31, 1911).

A patient in the ninth month of pregnancy stated that she had had a single pimple on the external genitals when two months pregnant, and that mucous patches had appeared during the fifth month. An intravenous injection of 0.4 Gm. of salvarsan was given, and in four days the mucous patches had disappeared; the only ill effect was a slight diarrhea, which continued till her confinement, ten days later. She was delivered of a living girl weighing 4380 Gm. and showing no syphilitic lesion. The placenta weighed 860 Gm., and had the appearance of minced pork. Six months after confinement the mother showed no symptoms of syphilis, having received a second injection six weeks after confinement. The baby at fourteen months was in good health. Oui (Écho méd., March 24, 1912).

Six pregnant women and eighteen infants treated with arsenobenzol. In women acquiring syphilis or showing secondary symptoms during pregnancy one may suppose that the fetus is not yet infected and that the administration of repeated salvarsan injections, in doses of 0.25 to 0.3 Gm., is therefore clearly indicated. In cases, however, that have not recently exhibited any symptoms of syphilis, and in which the sole aim is to avoid interruption of pregnancy by premature expulsion or fetal death, mercury and iodides are to be given the preference over salvarsan, except in cases not bearing mercury well, those in which the ordinary measures have failed at a former pregnancy, or where medication must be concealed. Fabre and Bourret (Lyon méd., Nov. 3, 1912).

The liver and kidney during pregnancy usually permit the elimination of the drugs without injury, yet there is always an element of uncertainty, and this is the special danger of salvarsan medication during pregnancy. Cases have been published in which the liver and kidneys seemed to be functioning normally and yet the balance was upset so easily that salvarsan caused serious injury. The variable findings with the Wassermann reaction indicate that salvarsan has no settled influence on syphilitic infection during gestation. Even when the reaction becomes negative under the medication it is liable to veer to positive again at any moment. The influence on the fetus is equally uncertain; the fetus may even give a stronger positive reaction than the mother. Sauvage (Annales de gynéc. et d'obstét., Jan., 1913).

Report of 9 cases in which pregnant women with syphilis were given salvarsan. In only 2 were there any syphilitic symptoms in the children, who were under observation from ten weeks to one year after birth. Some of the women had given birth during the previous two years to syphilitic infants. Treatment of the mother or the prospective mother exerts a very favorable influence on the vitality and development of the child. M. Holth (Deut. med. Woch., Bd. xxxix, S. 462, 1913).

Salvarsan Treatment in Congenital Syphilis.—Infantile syphilis can be favorably influenced by the administration of salvarsan to the nursing mother. Sometimes, however, the results thus obtained are harmful rather than beneficial, and in any event, subsequent direct treatment of the child, when its general condition has improved, is required. Immediate direct treatment of the syphilitic infant with salvarsan is attended with danger to its life, very probably owing to the sudden liberation of a large amount of toxins from the killed spirochetes, and should therefore not be attempted unless the child is already in a condition such that death is expected, *e.g.*, in **pemphigus neonatorum.**

Several syphilitic infants treated with the milk of syphilitic mothers that had first received a dose of salvarsan intravenously. There was some improvement of the symptoms, but not nearly as pronounced as the author had expected. In several cases an undoubted specific rash developed after the milk had been given. Analysis showed that there were appreciable amounts of arsenic present in the milk, but probably also some endotoxins and antibodies. It would be more rational to feed such infants with the milk of cows or goats that had received a dose of salvarsan. Jesionek (Münch. med. Woch., May 30, 1911).

Action of salvarsan in 26 cases of **syphilis** in infants and young children described; 13 were under a year old. The youngest was 5 weeks old. All were fairly well developed and nourished breast-fed infants. At first the initial dose was 0.005 Gm. (1/12 grain) per kilogram (2 1/5 pounds) of weight, but later this was increased to 0.008 Gm. (1/8 grain) and to 0.01 Gm. (1/6 grain) per kilogram. Wechselmann's neutral suspension was found satisfactory. Three injections were given in 1 case, two injections in each of 9 others. All but one of the injections were intramuscular. The increase in weight of the infants while under observation was fairly satisfactory. The children did not suffer from digestive disturbance as a result of salvarsan. Altogether three relapses were observed; in 2, in spite of the fact that Wassermann's reaction had become negative. The cutaneous manifestations of syphilis and those of the mucous membranes improved with wonderful rapidity. In 2 cases of **osteochondritis cubitorum** improvement was very rapid, and in 1 of them after two weeks, in the other after three, the symptoms had altogether disappeared. There was considerable improvement in a case of **syphilitic cerebral tumor** with **hydrocephalus** and already developing optic atrophy. Bokay (Wiener klin. Woch., Nu. 17, 1911).

Case of **congenital syphilis** in an infant treated with mercury. The Wassermann in both mother and child was positive. The mother was given 0.4 Gm. of salvarsan. Its effect on her was gratifying; she felt much better than she had for a long period. Seven days after the injection the Wassermann reaction in both parent and child was negative. No arsenic was found in the milk, examination of which showed it to be normal as regards fats and total solids. Twenty-five days after the injection the child died. Chapin (Amer. Jour. of Obstet.; Amer. Jour. of Dermat., Sept., 1911).

Report of a case showing provocation of syphilitic skin eruption in an infant through the milk of the mother treated with salvarsan; another case in which numerous efflorescences appeared where the skin had previously been normal twenty-four hours after the injection of salvarsan; a third in which a recurrent erythema multiforme and syphilitic efflorescences with the already existing exanthem followed the injection; and 2 cases in which salvarsan seemed to excite a pseudosclerosis. In the latter cases the differentiation between pseudosclerosis and a fresh infection was difficult. Oppenheim (Wiener klin. Woch., Oct. 5, 1911).

Salvarsan may prove very beneficial in the syphilitic child born at term. It acts very promptly on **pemphigus** and causes rapid disappearance of spirochetes from pemphigoid lesions. It is capable of producing prompt and lasting recovery from **hydrocephalus** of syphilitic origin. Disappearance of the phenomena of **syphilis,** even when associated with a negative Wassermann, does not imply a permanent cure. It is possible that salvarsan lowers the resistance of the newborn infant to intercurrent infections. Only 0.01 Gm. (1/6 grain) for newborn infants should be used, repeated twice or thrice at six-day intervals. P. Bar (Bull. de l'Acad. de Méd., Oct. 31, 1911).

In syphilitic infants salvarsan was found to overcome rapidly **pemphigus,** all mucous patches, and **chronic coryza.** Its effect in improving the general condition was, however, far less constant. In cases not presenting any syphilitic manifestations except poor general condition, salvarsan should not be used unless mercury and iodides have failed. Where it is employed, its effects are evanescent; mercury and iodides should always be given afterward and the salvarsan not repeated until acute eruptive phenomena return. The authors recommend, in infants, intramuscular injections of neosalvarsan, 0.05 Gm., not into the most fleshy part of the buttock, but into the muscles covering the external iliac fossa. The needle is introduced to the bone, then withdrawn slightly, so that its point shall lie in the muscle. Since dressings at this area in infants cannot be kept clean, the puncture is merely covered with a little cotton, dipped in collodion. Fabre and Bourret (Lyon méd., Nov. 3, 1912).

Forty children with **congenital syphilis** treated. The results observed from salvarsan and neosalvarsan intravenously were about the same. In poorly nourished children mercury should be given first, followed by salvarsan. Two pregnant mothers were treated with salvarsan and the infants showed a negative Wassermann reaction, but had some signs of latent syphilis. Dunzelmann (Zeit. f. Kinderheilk., Jan., 1913).

In children less than 6 years of age, it has been the practice to give intramuscular injections exclusively because of the difficulty attending intravenous procedure in these cases. The dose considered suitable has been 0.004 or 0.005 Gm. for each pound of the child's weight. La Fétra, however, has found it not inconvenient to administer salvarsan intravenously in these little patients, exposing the vein before injecting, and considers this method the best.

With correct technique the intravenous application of salvarsan in full-term infants as well as in premature births is the method of choice. In severe infections a rather large dose should be injected, that is, not under 0.04 Gm., and such a dose, from 0.04 to 0.1 Gm., will have no detrimental effects on full-term infants. In mild cases small doses should be used. In general the injection should be repeated and should be supported by other antisyphilitic remedies. Engelmann (Zentralbl. f. Gynäk., Jan. 20, 1912).

Eight milligrams (1/8 grain) per kilogram (2 1/5 pounds) of body weight intravenously is the maximum dose of salvarsan for infants. Where the infant is enfeebled it is better to give mercury or to begin with much smaller doses of salvarsan—3 to 5 mgm. (1/20 or 1/12 grain) per kilogram of body weight. If there be any sepsis salvarsan should be withheld. In removing the symptoms of the disease, salvarsan is more speedy than mercury. Combination of salvarsan with mercurial treatment, however, gives the best prospects of cure. C. T. Noeggerath (Jahrb. f. Kinderheilk., Feb., 1912).

Report concerning 25 cases of **congenital syphilis,** 10 of which received salvarsan with or without mercurial treatment, while 15 were treated by the use of mercurials alone. The mercurial treatment consisted of 1/4 to 1/2 grain (0.016 to 0.032 Gm.) of gray powder three times daily, together with inunctions of 25 per cent. blue ointment every second day. The salvarsan was given intravenously. The dose of salvarsan varied from 0.05 to 0.1 Gm. (3/4 to 1 1/2 grains). A febrile reaction was seen only three times and was very mild. There was never any necrosis or inflammation at the site of venipuncture. Of the 10 cases treated by salvarsan 2 ended fatally; all the others were decidedly improved with the disappearance of specific symptoms. Of the 15 cases treated by mercurials alone 3 improved, 2 did not improve, and 10 terminated in death. After the injection of salvarsan the Wassermann reaction was found to be still positive in 2 out of 3 cases in which the reaction was tested and in which the clinical symptoms had disappeared. While the indirect method of giving salvarsan to the nursing mother is valuable and should be used when the mother is available, the surest method consists in giving the salvarsan to the infant. Both indirect and direct administration should be employed whenever possible. The intravenous route of administration is the best. Usually it will be found easiest to expose the vein before attempting to insert the needle. The dose should be not less than 0.01 Gm. to the kilo of body weight.

Repeated injections and supplemental treatment by mercurials may be necessary. The Wassermann reaction should be followed for a year. La Fétra (Archives of Pediatrics, Sept., 1912).

Jesionek has introduced the method of giving infants the milk of goats to which salvarsan has been administered. This does away with the transmission to the infant of spirochetal endotoxins liberated when salvarsan is given to the mother, and avoids the injury to the child sometimes produced by the latter form of treatment. Jesionek's results have been good, but the procedure he advocates is not readily available—even were cows used instead of goats—and, on the whole, direct administration of salvarsan according to the usual methods is more effective.

The author injected 0.6 Gm. of salvarsan intravenously in a goat, and observed marked retrogression in the symptoms of **congenital syphilis** in a child to whom milk from this goat was fed. After a second injection of 1 Gm., the symptoms disappeared completely. Jesionek (Münch. med. Woch., May 30, 1911).

Report of a case of **congenital syphilis** in a child of 5 weeks treated with milk from a goat given seven injections of 0.3 or 0.4 Gm. of salvarsan into the jugular vein. The symptoms in the child improved slowly for a time, and then remained stationary, necessitating recourse to mercurial treatment. The milk showed no trace of arsenic. The amount present, if any, must have been not more than 1/10 mg. per liter. In Jesionek's case rapid improvement was reported, but the observations of the authors did not confirm this. Jeanselme, Vernes, and Bertrand (Paris méd., No. 1, 1911).

Manifestations of congenital syphilis in adolescents or young adults are relatively refractory to salvarsan. Gummatous processes may be quickly healed, but interstitial keratitis is not often markedly benefited, and syphilitic nervous phenomena are rebellious.

In Diseases Other than Syphilis.—In **yaws** (frambesia), due to the *Spirochæta pertenue,* salvarsan is even more effective than in syphilis. A single injection almost invariably cures it completely.

Five hundred cases of **frambesia** treated with injections of salvarsan, 498 being cured. Of these 409 were cured with one injection, 75 with two injections, and 14 with three injections. Of the 2 cases not yet cured, both show amelioration. There was an almost entire absence of complications. Other organic arsenic compounds, such as sodium cacodylate, arsacetin, etc., have no effect on yaws, and mercury has utterly failed as a remedy. Salvarsan is a specific for yaws, and there is no danger attending its use for this disease. Henry Alston (Brit. Med. Jour., Jan. 6, 1912).

Intramuscular injections of salvarsan given in 22 cases of **yaws,** with excellent results. The duration of the patients' stay in the hospital averaged twenty-five days, as against three months under other modes of treatment. But 1 case required a second injection. In 3 cases from which tissues were examined for spirochetes the latter were found to have disappeared within forty-eight hours after the injection. The stay of twenty-five days in the hospital was not necessitated by the treatment, but was due to the fact that practically all cases were infected with ankylostomiasis, and removal of these parasites was necessary as a preliminary to the treatment by salvarsan. R. P. Cochin (Jour. Trop. Med. and Hyg., Sept. 16, 1912).

The number of cases of **yaws** at a Trinidad hospital was reduced from 250 to 29 by the use of salvarsan. Henry Alston (Brit. Med. Jour., No. 2713, 1913).

Salvarsan is well borne by the stomach provided this organ be empty at the time of administration and that no food be taken for at least two hours after ingestion of the drug. In **frambesia,** at least, the therapeutic effects are the same as by the ordinary routes of introduction. Brochard (Soc. de Pathol. exot.; Presse méd., Jan. 29, 1913).

Salvarsan used with success in the treatment of **frambesia** among Congo natives. The lesions healed within ten days, and the joint nodositites which appear related to the disease were also favorably influenced. Mouchet and Dubois (Soc. de Pathol. exot.; Presse méd., Jan. 29, 1913).

Salvarsan used in 2 cases of **ulcus tropicum.** Each patient received an intramuscular injection of 0.5 Gm. suspended in olive oil. Complete cure took place rapidly in both cases. Hallenberger (Arch. f. Schiffs- u. Trop.- Hyg., Aug., 1912).

Treatment carried out on 36 cases of **oriental sore** (Leishmaniosis) by intravenous injections of salvarsan. There were 31 favorable results (16 cured, 4 nearly cured, and 11 much improved); 2 appeared to be unaffected, while the 3 remaining were not heard of after treatment. The drug was dissolved in distilled water and given in a dose of 0.4 to 0.6 Gm. for an adult. Of 15 cases completely cured, healing took place in fourteen days in 6 cases, in six days in 3 cases, in eight days in 2 cases, and in ten, eleven, nineteen, and thirty days in 4 cases. Salvarsan in these doses is a specific against the protozoa causing oriental sore. The dose may be repeated in a couple of weeks if improvement is delayed. P. v. Petersen (Münch. med. Woch., Nov. 12, 1912).

Gangosa patients at Guam were ordinarily treated with iodine mixture, but since the introduction of salvarsan this product has been given a trial, and it seems that if employed in the early stages it will prevent extensive destruction of tissue. It should however, be supplemented by a prolonged course of mixed treatment. Kerr (U. S. Naval Bull.; N. Y. Med. Jour., May 17, 1913).

Eight cases of **rat-bite disease,** occurring in various parts of Japan, treated with salvarsan. The drug was administered at different stages of the disease and also in the febrile and afebrile periods. Except in 3 cases, a single intravenous injection sufficed to prevent all further manifestations of the disease. S. Hata (Münch. med. Woch., Bd. lix, S. 354, 1912).

In **relapsing fever,** due to the *Spirillum obermaieri,* the parasites are caused to disappear from the blood in a few hours and the fever is aborted. Recurrence occurs only in about 2 per cent. of the cases if the drug be administered intravenously.

Report of 332 cases of **relapsing fever** in Indochina treated with an intravenous injection of 0.2 Gm. of salvarsan. There followed only 6 relapses, which yielded quickly to a second injection. In 24 cases there was a return of fever on the twelfth day without reappearance of the spirilla. This disappeared in one to three days. Mouzels and Nguyên-Xuan-Mai (Bull. de la Soc. Méd. et Chir. de l'Indochine, No. 7, 1912).

In **trypanosomiasis (sleeping sickness)** salvarsan is by no means a specific as in the two affections just referred to. The trypanosomes, after an intravenous injection, may disappear for a time, but recurrence seems practically inevitable. The drug possesses no marked advantage over the allied arsenicals, atoxyl and arsenophenylglycin, nor over antimony.

The relative toxicity of salvarsan and neosalvarsan to trypanosomes was tested by the authors. Neosalvarsan proved actively parasiticidal in dilutions up to 1 in 500,000 in half an hour. Similar experiments made with salvarsan, dissolved with the minimum amount of alkali, an amount which would not injure the parasites, showed that in a 1 in 100,000 solution the organisms were still very motile after half an hour. Neosalvarsan was thus shown to be five to ten times more actively parasiticidal than the older preparation. J. McIntosh, P. Fildes, and H. B. Parker (Lancet, July 13, 1912).

Filariasis may be benefited by salvarsan, the parasites being inhibited for a time and the patient's general condition improved.

Case with *Filaria sanguinis hominis,* with unilateral **chyluria,** treated by 0.6 Gm. of salvarsan administered hypodermically. The urine remained unchanged for the first twenty-four hours. During the succeeding forty-eight hours it became perfectly clear for the first time since the inception of the complaint, seven months before. Suddenly, however, from the sixty-eighth to the seventy-second hour, it became markedly chylous and contained large numbers of seemingly dead filariæ of both embryonic and adult forms. Then turbidity ceased until at discharge only an intermittent opacity was present, and no filariæ were demonstrable. Blood-smears taken continuously for one week were all negative as to filariæ, whereas before the injection there had been no trouble in finding the filariæ in the midnight specimens. P. M. and J. T. Pilcher (Med. Record, March 11, 1911).

Warning against the use of salvarsan in bilharziasis, which has not proved at all successful in its treatment. Looss (Deut. med. Woch., Jan. 11, 1912).

In **malaria** the drug is of little value except in the tertian variety, in which an absence of parasites from the blood for some weeks may result from its use. In cases refractory to quinine, salvarsan frequently proves beneficial, not only destroying the parasites, but overcoming the resistance to quinine, so that if the latter is used when the fever reappears its action will be more evident than before (McDonagh).

When salvarsan is introduced in a single dose of 0.5 Gm. intravenously in **tertian fever,** the parasites usually disappear after from twelve to forty-eight hours. The attacks cease. In quartan fever the action of the remedy does not last, even after a dose of 0.8 Gm. In the tropical form, doses of from 0.5 to 0.8 can only produce a temporary disappearance of the ring forms from the blood. The crescent form does not disappear, although it may become temporarily modified in shape and staining properties. In some cases of tropical malaria, a so-called contrary effect was noticed. After a temporary lowering of the temperature and diminution or complete disappearance of of the ring-shaped parasites from the blood, there took place a distinct turn for the worse in the patient's condition, with reappearance of rings and crescents in large numbers. Iversen and Tuschinsky (Deut. med. Woch., Jan. 19, 1911).

Neosalvarsan tried in 5 cases of tertian **malaria.** The plasmodia disappear quickly, but it is a question whether this is permanent. To avoid a recurrence one should give a second injection two days after their disappearance; even a third injection may become necessary. Iversen and Tuschinsky (Münch. med. Woch., July 16, 1912).

Salvarsan cures the benign tertian, but does not prevent the recurrence of malignant tertian **malaria.** The injection should be given at the beginning of the attack of fever, when the young forms predominate. In the 2 cases reported a rapid recovery was obtained in both after a single intravenous injection. In both cases a positive Wassermann was converted into a negative one by the treatment. R. Cestan and M. Pujol (Gaz. des Hôp. Civ. et Milit., Nov. 12, 1912).

Salvarsan in doses of 0.3 Gm. given in 3 cases of estivoautumnal **malaria.** The estivoautumnal parasite is not destroyed by this drug, but nevertheless in 1 case it was useful in preventing relapses. V. Fusco (Gazz. d. Osped. e d. Clin., Nov. 14, 1912).

In skin diseases salvarsan has been extensively tried, with varying results. In **psoriasis** and **lichen planus** the remedy is of distinct value, though not very evidently superior to arsenic in other forms. Cases of obstinate **pemphigus** have been benefited by it.

Salvarsan used in 3 cases of **psoriasis,** the dosage being 0.4 to 0.5 Gm. For a few days following injection there apeared to be some improvement, but after this the condition failed to improve. Schwabbe (Münch. med. Woch., Bd. lvii, Nu. 36, 1910).

Strikingly prompt improvement from an injection of salvarsan in an intractable case of **pemphigus.** During a year and a half the skin had never been entirely free from bullæ, the number present varying from twenty or more to several hundred. Arsenic in very large doses (40 minims of the liquor potassii arsenitis three times a day) had proved of some benefit, but nothing had ever prevented the development of bullæ, nor given more than temporary relief from pain. Salvarsan (0.6 Gm.) was injected subcutaneously in the scapular region. No new bullæ developed after the first twelve hours, and the skin was practically clear at the end of six days. R. L. Sutton (Boston Med. and Surg. Jour., March 9, 1911).

Two cases of **pemphigus** were very favorably influenced by salvarsan injections, while under the former treatment—quinine, Fowler's solution, zinc powder, and baths—no improvement had been visible. The dose was 0.6 Gm. given intravenously. Stümpke (Berl. klin. Woch., July 1, 1912).

In **lichen ruber planus** salvarsan seemed to act as a specific. A woman, 47 years of age, who received two injections intravenously, one of 0.3 and the other ten days later of 0.4 Gm., was cured of the disease after fourteen days. Polland (Wiener klin. Woch., Aug. 1, 1912).

In a case of **cancer of the tongue,** all other methods having failed, the author tried arsenobenzol, a dose of 0.5 Gm. being injected intramuscularly. In from thirty-six to forty-eight hours the pain disappeared, the ulcerations cleared, and the fetid discharge disappeared almost entirely. After ten or fifteen days these symptoms reappeared; a second injection was given six weeks later, and a third ten days after that. These later injections were both given intravenously, the dose being 0.3 Gm. each time. Although death supervened five months later from cancerous cachexia, the pain and the discharge had not reappeared. E. Bodin (La Clinique, Feb. 17, 1912).

In **pellagra** salvarsan seems to have been useful in a certain proportion of cases.

Twenty-one cases of **pellagra** treated with salvarsan by both intramuscular and intravenous methods, and in varying amounts, collected. Most cases had a single dose, 1 had two doses, and 2 were given three doses. There was an untoward result in 1 case, a profuse diarrhea following the injection. In 47.6 per cent. no improvement occurred. At least temporary improvement was observed in the remainder. The well-known dangers of administering salvarsan to patients suffering from cardiac and renal lesions contraindicate its use in many cases of pellagra, because of their well-known tendency to myocardial and renal degeneration. If given at all, it should be given in broken and repeated doses, and preferably by the intramuscular method. H. P. Cole and G. J. Winthrop (Jour. Amer. Med. Assoc., June 17, 1911).

Report of 27 cases of **pellagra** treated with salvarsan; of these 20 were apparently cured, 3 were doubtful, and 4 ended fatally. The author gives each patient doses of salvarsan varying in number from five to twelve at intervals of seven to ten days. The first dose was 0.2 Gm., the second 0.4 Gm., and subsequent doses were calculated on the basis of 0.1 Gm. for every 20 pounds of the unclothed patient's weight. Both syphilis and pellagra should be treated by giving intravenously doses of salvarsan until no reaction follows, *i.e.*, no fever, no vomiting, and no bowel disturbance. Pellagra cases require twice as many doses as the syphilitic.

Of the 4 deaths after salvarsan there seemed to be some connection in 3 of them between the reaction and a subsequent cerebritis or meningitis.

There appears to be but small choice in pellagra between salvarsan and sodium arsenilate, except that the latter must be given hypodermically during a period varying from eighteen months to two years. E. B. Martin (N. Y. Med. Jour., March 15, 1913).

In **scurvy** salvarsan has proven of some value, a distinct influence being exerted on the hemorrhagic manifestations and general condition.

The bad state of nutrition in buccal scurvy is due largely to the condition of the gums. Several intravenous infusions, usually of 0.3 Gm., were given to 8 cases. The results were remarkable in that the lesions of the mouth usually healed within a week and that the spirilla were much diminished in number, though they never disappeared enirely. The other symptoms of the disease were not, however, influenced; so salvarsan cannot be regarded as a specific for scurvy. Tusčhinsky and Iwaschengow (Münch. med. Woch., Dec. 12, 1911).

In rebellious cases of **noma** good results have been obtained.

It would seem advisable, even in the absence of positive evidence that spirochetæ are the specific organisms of **noma**, to make use of salvarsan in every case which does not immediately yield to local treatment. Nicoll (Archives of Pediatrics, Nov., 1912).

Chorea has been treated with salvarsan with asserted advantage.

Case of **chorea gravidarum** given an intravenous infusion of salvarsan two to three months before term. The patient was cured, no return of symptoms appearing, even after delivery. The method is to be recommended in severe cases which have resisted all other measures. Thus an interruption of pregnancy may be avoided, the efficacy of this procedure being doubtful. E. Härtel (Münch. med. Woch., Jan. 28, 1913).

Cases of **leukemia** have also been benefited temporarily or permanently.

In **pernicious anemia** the drug has proven strikingly effective in a fair proportion of cases, ineffectual in others, and harmful in a few.

Seven cases of **pernicious anemia** treated with salvarsan. One showed striking improvement, four injections of 0.3 Gm. each being given during six weeks, in which time the red cells increased from 1,760,000 to 3,350,000 and the hemoglobin from 52 per cent. to 78 per cent. During the year following the last injection the blood continued to improve, the red blood-cells increasing to 6,210,000 and the hemoglobin rising to 120 per cent. Five other patients showed more or less improvement, and in only 1 was no benefit derived. To secure the best results salvarsan should be given intramuscularly, on account of the prolonged action which results. Salvarsan will probably be found a more efficient remedy than arsenic given by the mouth, and indeed more efficient than any form of treatment which has yet been employed in pernicious anemia. Bramwell (Brit. Med. Jour., June 22, 1912).

In **pernicious anemia** the intravenous injection of salvarsan produced such an anemia that the patients in 2 out of 3 cases died within three weeks, and the third patient was not improved, though he apparently was not damaged by the treatment. Both in chorea and leukemia not only did the injection of salvarsan not cure the disease, but it did not prevent the appearance of complications. Charteris (Brit. Med. Jour., Sept. 21, 1912).

Case of a woman who had been anemic for more than a year. A blood-smear showed typical **pernicious anemia.** Salvarsan, 0.3 Gm., was injected intramuscularly. Within three days benefit was apparent, although local pain was severe for about a week. In four days the hemic murmurs had almost disappeared, and the patient was much stronger. Blood examination showed a distinct improvement, and two weeks later the same dose was again injected; this was followed by a sharp reaction; the temperature rose to 101° F. (38.3° C.). The patient looked exceedingly ill; the pallor and hemic murmurs returned, and she developed a large patch of dry pleurisy. This condition lasted a few days, when the fever slowly subsided and uninterrupted recovery set in. E. Hobhouse (Brit. Med. Jour., Dec. 14, 1912).

Case of **pernicious anemia,** in which 0.3 Gm. of salvarsan was given intramuscularly. There was a definite increase in the number of red cells for a fortnight, when a second dose was given. Examination of the blood a week later revealed a diminution in the red cells; the treatment was therefore stopped. E. F. Maynard (Brit. Med. Jour., Jan. 11, 1913).

In a case of **Banti's disease,** with typical liver and spleen and characteristic blood-count, the author obtained a cure after a subcutaneous injection of 0.4 Gm. of salvarsan. The nodules in the liver disappeared completely and the spleen slowly returned to its normal size. The only thing remaining is a leucopenia with relative lymphocytosis. The patient, a boy 14 years old, gave a distinct history of congenital syphilis. Many cases of Banti's disease are syphilitic in origin. It is the physician's duty to perform the Wassermann reaction before turning a case of Banti's disease over to the surgeon. W. Schmidt (Münch. med. Woch., March 21, 1911).

Case of a woman, aged 30 years, with very marked anemia, marked enlargement of both liver and spleen, edema and suffering from persistent vomiting and diarrhea. The patient received three intravenous injections of 0.3 Gm. of salvarsan during a period of four weeks, and was apparently cured. Perussia (Münch. med. Woch., Bd. lix, S. 1482, 1912).

Report of the case of a man, 22 years of age, who suffered from **splenic anemia,** together with tuberculosis and malarial infection. This patient received two injections of salvarsan intravenously, 0.15 and 0.4 Gm.; he progressed favorably, and the author expects a cure, having just given a third injection of 0.4 Gm. Vallardi (Münch. med. Woch., July 2, 1912).

Report of a case of **splenic anemia** in an adult, treated with salvarsan. The result was good. Every patient whose case has been diagnosticated as Banti's disease should receive an antiluetic, especially salvarsan, even if the Wassermann reaction remains negative. Curschmann (Münch. med. Woch., July 2, 1912).

In **sympathetic ophthalmia** marked benefit from salvarsan has been reported.

Good results from the use of salvarsan in **sympathetic ophthalmia,** the blood count becoming normal and the eye quiet. S. H. Browning (Ophthalmoscope, Nov., 1912).

Case in which an iridectomy had been performed on an eye badly injured by iritis. Seven days later the other eye showed distinct symptoms of a commencing **sympathetic ophthalmia.** The eye operated on was enucleated at once, the patient placed in bed, and the usual treatment begun, but the eye constantly grew worse. Finally, although the Wassermann reaction was negative, 0.7 Gm. of neosalvarsan was given intravenously. Improvement began at once and proceeded to recovery. F. P. Calhoun (Amer. Jour. of Ophthal., April, 1913).

In **small-pox** salvarsan administered early in the eruptive stage will bring the rash to a standstill and ward off complications.

Salvarsan given in 3 cases of **small-pox.** It proved harmless and a favorable influence seemed to be exerted. Lenzmann (Med. Klinik, April 30, 1911).

By injecting 0.3 Gm. salvarsan intravenously in **plague,** the author increased the agglutinin of the serum to five times the original amount. No deadening effect upon the plague bacilli themselves is produced. Aumann (Deut. med. Woch., Nov. 14, 1912).

In **scarlet fever** salvarsan has been tried with asserted benefit.

Salvarsan treatment given in a series of 39 cases of **scarlet fever** of severe type; 5 cases died, a mortality of 12.6 per cent. as compared with 24.5 per cent. mortality in 44 cases not treated with salvarsan. One of the fatal cases was an instance of puerperal scarlet fever following a septic abortion, death being due to sepsis. Another occurred in a 2-year-old child who had whooping-cough and died of bronchopneumonia. Two other cases when admitted suffered from severe diphtheritic and streptococcic toxemia. Only 1 of the 5 fatal cases was thought to be due to actual scarlatinal infection. The percentage of complications was much smaller in the cases treated with salvarsan. Thus, otitis media developed in only 6.6 per cent., as compared with 14.3 per cent. in the untreated cases; nephritis occurred in 25 per cent., as against 43 per cent.; and endocarditis was observed in 3 per cent., instead of 16 per cent. The effect of the remedy was marked upon the course of the disease. In all but 2 cases the temperature fell by crisis shortly after the injection. This fall was followed by a rise on the following day, but seldom to the original height of the fever. A few of the patients received a second injection of salvarsan. The doses given were 0.1 to 0.2 Gm. to infants, 0.3 Gm. to older children, and 0.5 Gm. to adults. Most of the injections were given intravenously and only were given in highly diluted form intramuscularly when intravenous injections were impossible. Klemperer and Woita (Therapie der Gegenwart, Bd. viii, S. 198, 1912).

Salvarsan used in 109 and neosalvarsan in 8 cases of **scarlet fever.** Upon the throat symptoms, especially in the necrosing form, a strikingly favorable effect was produced. The necrotic lesions began to clear up with unexpected rapidity, this probably accounting for the small number of the cases in which otitis appeared. Sequelæ such as glandular enlargements and nephritis, on the other hand, were not warded off by the remedy. The milder cases of scarlatina do not require salvarsan treatment, which is indicated, however, in the severe toxic forms. *Neo*salvarsan is not suitable for the treatment of scarlet fever. G. Jochmann (Congress on Internal Medicine, Wiesbaden; Zentralbl. f. inn. Med., May 31, 1913).

In **anthrax**, experimental and clinical, trial of salvarsan seems to have shown it to be a remedy of some value.

Case of **anthrax** in which the prognosis, according to past experiences, seemed absolutely unfavorable. An intravenous injection of 0.6 Gm. of salvarsan was given and recovery followed. G. Becker (Deut. Zeits. f. Chir., Bd. cxii, 1911).

Experiments with salvarsan on animals infected with the **anthrax** and **erysipelas bacilli.** The good effects are due to the proved property of salvarsan, of increasing the antibodies in the animals. Bierbaum (Deut. med. Woch., Oct. 24, 1912).

Experiments with salvarsan in rabbits infected with **anthrax.** Sources of error carefully excluded. In the dose of 0.04 Gm. per kilo of animal salvarsan was found capable of saving animals otherwise doomed to succumb from virulent strains of the bacilli. While the author cannot affirm that in Becker's human case the drug saved life, he advises that in serious cases of anthrax salvarsan be given. G. Schuster (Ehrlich's "Abhandlungen über Salvarsan," Bd. iii, 1913).

Case of a man severely infected with anthrax. He had a large swelling about the size of the fist on the right side of the throat and on it was a spot with a dark crust, surrounded by many pustules. There was also enlargement of the neighboring lymphatic glands. The pus was found to contain anthrax bacilli. Morning temperature, 100.8° F. (38.2° C.). The abscess was opened by the actual cautery. An intravenous injection of salvarsan was then given. After three hours the temperature had risen to 103.6° F. (39.7° C.), but at the end of eight hours it had dropped to 100.4° F. (38° C.). On the following morning the temperature was 97° F. (36.1° C.) and the patient's general condition much improved. The swelling was greatly diminished. After six days the infiltration of the glands and skin had disappeared and on the tenth day the crust fell off. The patient felt well after the second day. No anthrax bacilli were found in blood withdrawn by hypodermic needle. Salvarsan was the principal factor in the cure. It is to be preferred to the usual method of phenol injections around the carbuncle. Mokrzecki (Münch. med. Woch., May 20, 1913).

Finally, in **leprosy** salvarsan has been found capable of giving temporary relief in a number of cases. It is in no sense curative.

Nineteen **leprous** patients under salvarsan treatment for eighteen months. The drug was given intravenously in doses of 0.5 to 0.6 Gm. The only ill effect following was an exacerbation of the neuritis in anesthetic cases. In 2 anesthetic cases salvarsan was unsuccessful, and except in the very early stages the drug should not be employed in this condition. But in lepra tuberosa the effects are very gratifying, especially in the less advanced stages of the disease. Lepromata recede in size and degenerate, and the bacilli they contain are reduced in number. In affections of the mucous membranes, especially of the larynx and pharynx, benefit is very marked. The general condition of the patient is always greatly benefited, with a return of interest and energy. On the other hand, nervous symptoms show no change for the better, and little effect is produced on ulcers due to trophic interference. The Wassermann reaction remains unchanged throughout. J. P. Rocamora (Lepra, Sept., 1912).

In 4 or 5 **leprosy** patients administration of salvarsan resulted in clinical improvement. The other case ended fatally from the result of accidental burns before observations could be completed. Two cases in which the disease was least advanced showed the best results One of the controls remained unchanged in condition and the other grew steadily worse and finally died. In 1 case, *Bacillus lepræ* disappeared from the nasal secretion after treatment. Four patients showed partial or complete resolution of the specimen nodules examined after treatment. Wellman (N. Y. Med. Jour., Nov. 16, 1912).

Local Uses.—Salvarsan has been applied to the throat in **Vincent's angina** with marked success.

Vincent's angina may be favorably affected by the use of salvarsan. The drug may be applied directly to the lesions in powder form or may be mixed with glycerin and applied on a tampon. The applications are made twice a day. In from three to five days in most cases the cure is complete. J. Anglada and P. Reveille (Progrès méd., Feb. 15, 1913).

The author recommends in severe cases of **Plaut-Vincent angina** general salvarsan treatment, together with the local application of salvarsan glycerin. J. Citron (Berl. klin. Woch., April 7, 1913).

It has likewise proven useful in various other non-syphilitic buccal disorders.

Report of 16 cases of **scarlet fever** in which ulcerative and gangrenous complications were particularly serious. Salvarsan was employed, generally in the form of local applications of 1:10 or 1:20 solutions in glycerin, and sometimes intravenously. The action of the drug was very prompt and marked, 7 recoveries occurring among 12 especially grave cases. In 1 case of **noma** terminating fatally, the buccopharyngeal lesions had been cured, and death was due to a gangrenous focus in the lung. Netter (Bull. et Mém. de la Soc. Méd. des Hôp. de Paris, No. 25, 1912).

In the treatment of a case of **chronic superficial glossitis** 1½ grains (0.1 Gm.) of salvarsan were dissolved in ½ ounce (15 Gm.) of glycerin, of which quantity about a half was used in hourly swabbings over ten hours. The patient had been under careful medical treatment on and off for seven years, had given up smoking for short periods, and had improved under these treatments temporarily, but he asserted that his tongue had never been so comfortable or looked so well for ten years. At the end of one week, and after only two days of salvarsan, the ulcers had diminished to one-fourth their size. There was no history of lues. A. A. Allport (Brit. Med. Jour., Aug. 17, 1912).

Local applications of from 5 to 10 per cent. watery or glycerin solutions of salvarsan and neosalvarsan in spray form in the local spirochetoses (such as Vincent's angina, **ulitis simplex, stomatitis, noma,** and **alveolar pyorrhea**) advised. In these cases it is ordinarily a specific. The intravenous injection should be reserved for the severe cases accompanied by general symptoms. Gerber (Münch. med. Woch., March 25, 1913).

Many kinds of **ulcers** heal quickly after a single dusting with neosalvarsan or salvarsan diluted with xeroform (tribromophenol bismuth) in the proportion of 1 to 3. The after-treatment is a daily dusting with xeroform lightly sprinkled on. Water or lotion is not allowed to touch the sore. Salvarsan mixed with bismuth subnitrate was tried in 3 cases and found satisfactory. The ulcer was protected with loosely applied lint. The surrounding skin may be painted twice with tincture of iodine. The patient is kept in bed for one day. Henry Alston (Brit. Med. Jour., No. 2713, 1913).

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DIPHTHERIA.—DEFINITION.

—Diphtheria is an acute infectious and contagious disease produced by the presence and development of the Klebs-Loeffler bacillus. As it occurs in man, it is usually characterized by the presence of false membranes upon the surfaces primarily attacked, especially the mucous membranes of the nose, pharynx, larynx, or trachea. There can no longer be any question of the specific relation between the great majority of cases of the disease known since the time of Bretonneau as diphtheria and the bacillus with which Klebs and Löffler have identified their names. The bacillus is regularly obtained in cultures from affected throats; it can readily be isolated, and when pure cultures are injected in animals they reproduce the essential features of the disease met with in man. Welch and others, by inoculating the mucous membranes of guinea-pigs, have even succeeded in producing the false membranes so closely associated with the disease in man. All the constitutional effects and characteristic lesions, except the formation of membrane of diphtheria, have likewise been produced by the injection in animals of the toxins produced by the specific bacillus. In experimental diphtheria, induced either by the injection of cultures of the Klebs-Löffler bacillus or of its toxins, the most striking feature is the production in animals of the paralyses due to nerve and muscular degenerations, such paralyses reproducing most exactly the phenomena so often observed in clinical diphtheria. This feature of the experimental process has so impressed itself upon those most interested in laboratory researches that some propose to define diphtheria as an acute infectious disease produced by the action of the Klebs-Löffler bacillus, and characterized by the development of nerve degenerations.

While this teaching may be most in harmony with the combined evidence of clinical observation and laboratory research, it does not yet seem advisable to so far depart from the conceptions of diphtheria which have heretofore obtained. The appearance of false membrane has long been regarded as almost diagnostic; it still belongs to the great majority of cases, and can readily be appreciated, while the nerve degenerations, if they appear at all in clinical diphtheria, are met with only in the later stages of the disease, long after the question of diagnosis will have been determined.

VARIETIES.—The classification of the acute inflammations affecting nose, throat, etc., has not yet reached a satisfactory stage. The distinctions based upon the presence or absence of pseudomembranes have lost their significance.

While the great majority of pseudomembranous inflammations of these parts are due to the action of the diphtheria bacillus, a considerable number of such inflammations are produced by the action of other bacteria, especially the streptococci and staphylococci. On the other hand, the action of the diphtheria bacillus is not always attended by the production of pseudomembranes. The intensity of the local action of the bacilli varies greatly, and it has been found that this diphtheria bacillus may be the cause of simple inflammatory processes, formerly designated as catarrhal, which present no appearance of false membranes. Moreover, we find that the all-important question in any case, both with reference to prognosis and treatment, is the presence or absence of the diphtheria bacillus. We, therefore, abandon the former classification into catarrhal and pseudomembranous processes and speak of:—

1. *Diphtheria,* or *true diphtheria,* in which we include all cases of acute inflammations affecting mucous membranes associated with the presence of the diphtheria bacillus in sufficient number to constitute a probable causative agent. Thus, if a culture from a sore throat shows the presence of the diphtheria bacillus, that case is at the present time accepted as diphtheria, whether there be or not pseudomembrane present, and no matter what other bacteria be associated in the culture with the diphtheria bacillus. It must, however, be noted that the presence of the diphtheria bacillus without further clinical evidence does not constitute diphtheria any more than the presence of pneumococci in the mouths of healthy persons constitutes pneumonia.

2. *Pseudodiphtheria,* in which we include all cases resembling diphtheria, but not showing the presence of the diphtheria bacillus in cultures from the affected parts. Such pseudomembranous inflammations are commonly seen as complications of the acute infectious diseases, especially scarlet fever and measles. Cultures from such cases regularly show streptococci, or staphylococci, or both. The streptococci are especially frequent. Pneumococci and other bacteria have been found.

Outbreak in a girls' school of sore throat, bacteriologically proved due to a form of Klebs-Löffler bacillus, the resulting illness, however, failing to present the typical features of classical diphtheria. It might have been termed a "diphtheritic fever," the symptoms of which were as follows: A more or less severe coryza; a moderate tonsillitis, usually one-sided, and unattended by high fever or by much exudation; thickly coated tongue and foul breath, the tongue desquamating as in scarlatina; a patchy or punctate rash on the roof of the mouth and buccal mucous membrane; swelling of the cervical lymphatic glands; a roseolar rash on the skin (in 12 out of 18 cases—in 4 cases early in the attack, in 8 cases on the fifth to the seventh day from the first symptoms or invasion); distinct desquamation (in 3 cases), the peeling being particularly marked on the hands. Moore (Dublin Jour. of Med. Sci., Jan., 1908).

The site of the diphtheritic process, whether nose, tonsils or pharynx, or larynx, materially affects the symptoms and course of the disease; we, therefore, in our description, speak of *nasal, pharyngeal, or tonsillar, and laryngeal diphtheria.* In the effort to further classify their cases some divide them upon the basis of the bacteriological findings in cultures from the throat. Thus, when the culture shows diphtheria bacilli practically alone, they designate the case as bacillary diphtheria; when cocci are present in considerable numbers with the diphtheria bacilli, as coccobacillary diphtheria, etc. This method would be highly satisfactory did the clinical course and outcome of the disease correspond to the bacteriological findings, but they do not. The presence of cocci in the cultures does not show that they will play any important part in the disease, and the complications produced by their action—such as pneumonia and nephritis—seem to be as frequent in cases that give apparently pure cultures of the diphtheria bacillus from the throat as in those that show many cocci as well. When we have to do with a systemic infection with streptococci as well as the diphtheria bacilli, we speak of the cases as "mixed infections"; but the distinction is based upon the clinical symptoms of the disease and not upon the results of the bacteriological examination. We find it most advantageous to divide the cases into mild, severe, or septic, according to the character of the symptoms presented.

Corresponding to these three forms of diphtheria, Monti presents a classification based upon the character of the exudate in the throat:—

1. A fibrinous form, in which the diphtheritic products are only placed upon the mucous membrane, not incorporated with it. Virchow, Weigert, and Cohnheim call this the croupous form.

2. A mixed form, called also the phlegmonous form, in which the fibrinous exudate lies deep in the tissues as well as upon the mucous membrane.

3. A septic, or gangrenous, form, in which a fibrinous pseudomembrane is formed in the deep tissues of the mucous membrane, the process really consisting of a necrosis of the tissues and a mingling of the dead particles with the diphtheritic products.

Similar classifications are presented by other Continental writers; but we have not yet found it of advantage to attempt to classify our cases by the local appearances of the throat. Certainly the distinctions that Monti makes call for very nice and rather difficult discriminations.

SYMPTOMS.—These vary sufficiently with the site of the lesions to make it of advantage to consider the local forms separately.

1. **Nasal Diphtheria.**—Diphtheria of the nasal cavities is, in most cases, simple extension from the fauces or larynx. It may, however, occur as a primary affection. It is characterized by more or less complete obstruction of the nares, a thin, mucopurulent, and often bloody discharge from the nostrils, and a more or less marked toxemia. Pseudomembrane may be developed and may be visible through the anterior nares, but, as a rule, we see no membrane. The nasal discharge is usually very irritating, and the nares become excoriated. There is usually enlargement of the submaxillary lymphatic glands.

The degree of the toxemia varies markedly. Usually it is very moderate, the temperature is not high (100° or 101° F.—37.8° or 38.3° C.), the prostration is not marked, and the chief danger of the cases seems to lie in an extension of the process by continuity of tissue, to the pharynx or larynx, or the development of pneumonia.

The affection is often protracted, the discharge from the nose and the obstruction persisting for weeks, despite careful treatment.

Lennox Browne reported a total mortality of 63.4 per cent. in a series of cases of diphtheria involving the nose, and attributes to the nasal affection more importance than to the laryngeal. Few writers or clinicians can agree with this opinion. In practically all the cases of the series reported other parts were involved besides the nares, and the mortality record is a tribute to the gravity of extensive diphtheria rather than to the danger of the nasal affection alone. In infants, however, nasal diphtheria frequently proves fatal. It may readily be the origin of a pharyngeal or laryngeal process. It may, furthermore, be the means of communicating the disease to others.

A large percentage of all patients with faucial diphtheria admitted to hospital have a history of rhinorrhea. In a certain number of cases, which clinically are purely faucial, rhinorrhea is an early symptom, subsequently disappearing without treatment. The frequency of this early and transitory rhinorrhea bears a direct relation to the mildness and an inverse relation to the severity of the faucial attack. Faucial cases which are also clinically nasal are more severe than those which are clinically faucial only. Faucial cases which are also clinically nasal as a rule develop the nasal discharge at a later date than those which are clinically faucial only. Early and transitory rhinorrhea is relatively more common in laryngeal cases than in the faucial. Rolleston (Med. Press and Circular, July 3, 1907).

Primary nasal diphtheria is a more common disease than is ordinarily supposed. It is usually a benign affection, the constitutional symptoms being not marked, or even entirely absent. The primary form is very seldom malignant *per se,* and especially is this true if it remains confined exclusively to the nares. It displays a tendency to limit itself to the nose. When it does spread to portions of the respiratory tract lower down, the severity, that is, the toxemia and systemic disturbance, seems to increase *pari passu* with and as a direct result of such extension. There is a decided tendency toward chronicity. The prognosis is, as a rule, good. Paralytic phenomena, such as loss of knee-jerks, paralysis of the palate, etc., are extremely rare. It is capable of acting as a focus of infection, and the resulting cases may be of a malignant type. The importance of early detection of this disease by bacteriological examinations of all cases of persistent purulent rhinitis of doubtful origin, especially in children, cannot, therefore, be overestimated. G. W. Stimson (N. Y. Med. Jour., Dec. 14, 1907).

In 9 cases of apparently simple coryza in infants, with or without slight fever, bacteriological examination revealed a primary diphtheria, localized exclusively in the nose. **Antitoxin** rapidly cured the little patients. There is no doubt that primary diphtheria is comparatively common among babies, and bacteriological examination is necessary in every case of persisting catarrh. DeBiehler (Arch. de méd. des enfants, Nov. 1911).

2. Pharyngeal, or Tonsillar, Diphtheria.—*(A) Mild Cases Without Membrane, or Catarrhal Diphtheria.*—During the prevalence of an epidemic of diphtheria, especially in institutions, a certain number of cases may be observed in which, without the appearance of pseudomembrane, the pharynx and tonsils become reddened and somewhat swelled, the children complain of slight soreness of the throat and have a rise in temperature, but do not appear or feel very ill; yet, cultures made from such throats show the presence of the diphtheria bacillus. Such cases we have learned to class as true diphtheria. The mildness of the affection is attributed either to the small number of bacilli present, to a diminution in the virulence of the bacilli, or to an increased resistance on the part of the patient. In many of these cases the nose is involved as well as the pharynx and tonsils, and there is consequently a thin, watery, irritating discharge from the nostrils. In the course of a few days all symptoms subside, and the bacilli disappear, or they may persist for weeks without further symptoms.

The bacilli derived from cultures from such cases may prove to be fully virulent, and any such case may readily be the means of communicating a severe or virulent type of the disease to others.

The patients themselves may show albuminuria during the course of their mild attack, or they may later develop the paralysis belonging to the severer types of diphtheria. The latter outcome is, fortunately, rare.

From the catarrhal process in the throat and nose there may arise by extension a diphtheritic laryngitis either catarrhal or pseudomembranous in character, which may be followed by stenosis or other grave symptoms.

(*B*) *Mild Cases, With Membrane, of Pharyngeal, or Tonsillar, Diphtheria.*—These cases are characterized by the development of more or less pseudomembrane upon the tonsils, fauces, or pharynx and a moderate toxemia. The onset of the trouble is marked by sore throat, a moderate fever, 100° or 102°, and a slight prostration.

Upon examining the pharyngeal cavity we usually find one or both tonsils reddened, swollen, and presenting upon their surfaces one or more patches of pseudomembrane. These patches may be small and difficult to distinguish from the yellow plugs seen in follicular tonsillitis. The membrane is usually firmly adherent to the underlying tissue, and, if removed, leaves a bleeding surface. The area covered by membrane may sometimes be marked off from the surrounding tissues by a zone of congestion. The membrane is usually white-gray or grayish green in color, sometimes yellow, and the patches are of irregular form. It is sometimes thick and heavy, sometimes so thin as to be translucent.

In contradistinction from this description of diphtheritic membrane we might set the characters of pseudomembrane not diphtheritic, but the more painstaking the description, the more evident would it become that it is perfectly impossible to distinguish one from the other by simple inspection. Nothing short of a bacteriological examination will enable us to make the distinction with certainty.

With such appearances in the throat there is usually a distinct swelling and tenderness of the submaxillary and cervical lymph-nodes.

The extent of membrane in the mild cases is usually limited, and there seems little tendency toward spreading; but, on the other hand, we may see cases in which tonsils, fauces, and pharynx are covered with membrane and yet the constitutional depression is slight.

After the onset in a mild case the membrane may extend somewhat, so as to involve the fauces or pharynx; but may remain limited to the tonsils. The throat continues sore, the temperature shows some elevation, and the children feel moderately sick. In the course of three to five days the membrane begins to separate, either gradually or in masses, the throat clears up, the temperature falls, the glandular swelling subsides, and in a week or so the patient is well again.

A mild diphtheria may be accompanied by albuminuria, and may be followed by nephritis or paralysis, but, as a rule, the cause is benign and the outcome satisfactory. We must, however, be prepared at any time to see an apparently mild case of diphtheria change character and become a virulent infection. From a mild tonsillar, or pharyngeal, diphtheria a severe diphtheritic laryngitis may be developed.

The most troublesome features of these mild cases of diphtheria is the difficulty of maintaining proper quarantine. If adults, the patients do not regard themselves sick after the first day or two, and can hardly be made to understand that, even when well, they may be the source of grave danger to others.

If the patients are children, the parents find it difficult to take a serious view of an apparently trifling sore throat, and are often unwilling to take the necessary precautions to prevent the spread of the disease. It cannot be too emphatically laid down in such cases that the clinical phenomena are no test of the virulence of the bacteria present. From an apparently mild case Park obtained the most virulent bacillus he has yet met with, and employed its toxins in the production of antitoxin of unusual strength. It has, likewise, long been well known that an apparently mild case of diphtheria may communicate a malignant infection to others.

The mild cases should be quarantined just as faithfully as the most severe, and should be allowed freedom only when the specific bacteria have disappeared from the throat.

(*C*) *The Severe Cases.*—In these the manner of onset may be sudden, with chill, vomiting, fever, and severe sore throat, the temperature rising to 103° to 104° F. (39.4° to 40° C.), and the prostration being marked, or the affection may begin as a mild case and gradually develop the severe symptoms, the invasion being very insidious. If seen at the beginning, there may be little membrane visible in the throat, only a small patch or two upon the tonsils, exactly similar to that described in the mild cases; the throat will, however, be more reddened and the swelling more marked. The submaxillary and cervical lymph-nodes will be swollen and tender. The child looks and acts sick. The elevation of temperature may not be in keeping with the degree of constitutional depression, oftentimes being only 101° to 102° F. (38.3° to 38.9° C.). As the disease develops, the membrane rapidly extends, until the tonsils, pharynx, uvula, and fauces are covered with a thick gray, green, or even black layer of necrotic material. If any effort be made to remove it the underlying tissues bleed freely. The membrane fills the rhinopharynx, involves the nasal cavities, and may even appear in the nares. With the involvement of the nose there is seen a thin, acrid, often bloody and foul-smelling discharge from the nostrils. The membrane may also invade the mouth and appear upon the lips. In one case seen at the Foundling Hospital, the extent of gray membrane upon the lips, cheeks, and tongue was so marked as to suggest the possibility that the child had been drinking carbolic acid. Mechanical removal of the membrane in such cases does no good whatever; it seems only to open up a fresh surface to the attack of the virulent bacilli, and the membrane is reproduced with almost marvelous rapidity. At any time the inflammatory process may involve the larynx, giving rise to laryngeal diphtheria, or it may involve the middle ear through the Eustachian tubes; in rare cases by extension through the lachrymal duct or by accidental inoculation the conjunctiva is involved.

With the increase in the local process the lymph-nodes of the neck become more swollen and tender, until it seems that they will surely suppurate, but they rarely do so. The constitutional depression becomes more and more marked. The pulse becomes more rapid and feeble; the strength fails steadily.

> Irregularity of the pulse in diphtheria in children is really of little special significance, being due to the great incidence of the disease in the early years of life, especially the fourth and fifth years. Children at this age commonly exhibit this symptom in any febrile disturbances and often in apparent health.

The irregularity is very common indeed, it being found in over 80 per cent. of the author's cases. Comparisons of similar numbers of diphtheria and scarlet-fever cases showed about the same percentage of cardiac irregularity. The irregularity is referred by various authorities to a nervous origin rather than a cardiac. There seems to be an excessive susceptibility in the inhibitory action of the vagus, and it is believed that the rhythmical stimulation of the respiratory center has a rhythmical effect on the vagus center. The author refers to Barr's explanation of the mechanical effect of the respiratory act on the circulation. The fall in blood-pressure in disease is undoubtedly the primal cause setting up the irregularity.

If actual myocarditis is present an irregular pulse is of course of the gravest significance. In most diphtheria cases with irregularity the latter continues during hospital stay and the children are kept in bed week after week when they would do better if in the open air, which would certainly improve their anemia. Assurance must first be obtained that the irregularity is more than respiratory. The presence or absence of cardiac signs will help decide this point. O. H. Peters (Lancet, Sept., 14, 1907).

The temperature may not at any time be very high, 101° or 102° F. (38.3° or 38.9° C.), or it may reach 103° or 105° F. (39.4° or 40.5° C.). The swelling and tenderness of the throat render swallowing painful and sometimes almost impossible. The tonsils may almost meet in the median line; the nostrils may be plugged, and even respiration seriously interfered with. At times in the early days of the disease we may see fluids regurgiate through the nose, when any attempt to drink is made, and it may be difficult to determine whether the regurgitation is due to the obstruction of the throat by swelled tonsils or to early paralysis of the pharyngeal muscles.

As the diphtheria advances, the urine becomes scanty and high colored, and contains albumin in some quantity; at times an acute exudative nephritis is developed, with large quantities of albumin, casts, and even blood. The onset of the complication may bring, in its train, all the symptoms of an acute nephritis.

Although renal complications occur in the course of diphtheria, it is only in some few cases that they produce symptoms which cause immediate anxiety. In the large majority, they possess very little importance so far as the immediate future is concerned. They are perhaps more frequent in cases of great severity, but in these the severity of the dangers incidental to diphtheria overshadows the importance of the renal complications. The renal changes may be an evidence of severe toxemia, but, if death ensues, it will in general result from some cause wholly unconnected with the renal functions. Nestor Tirard (Practitioner, Jan., 1909).

Study of the blood-pressure. The maximum blood-pressure of normal children, according to Seiler, who used the Riva-Rocci instrument, is 75 to 80 mm. from 2 to 3 years; 79 to 90 mm. from 4 to 5 years. Cook and Briggs found slightly higher figures with their modification of the Riva-Rocci, and place them at 75 to 90 mm. up to 2 years, and 90 to 110 mm. after 2 years. Of the 179 cases observed by Rolleston, 63, or 35.1 per cent., according to Cook and Brigg's estimate, and 45, or 25.1 per cent., according to Seiler's figures, showed for varying periods a pressure below the normal. The varying degrees of depression bore a direct relation to the severity of the attack, being pronounced in severe and slight in mild cases. In the very severe class, of 22 cases, 18 according to Cook, and 17 according to Seiler, showed from 5 to 45 mm. below normal. The fall in pressure occurred rapidly and steeply, there being at times 10 mm. difference between the morning and evening readings. A difference of the reading of the two wrists indicated a grave prognosis. The severe and the moderate class of cases showed a considerable fall, but less marked than in the very severe class; the severe class showing 25 and 16 cases respectively, with fall of from 3 to 24 mm., and the moderate class 11 and 6 respectively, showing a fall of from 1 to 14 mm. Rolleston (Brit. Jour. Dis. of Children, Oct., 1911).

The mind may remain clear throughout; but, as a rule, with the deepening of the toxemia the patients become dull and listless. In the severest cases stupor or delirium may be developed. Coma is rarely seen. Convulsions may occur either early or late in the disease, from the toxemia of the diphtheria or from uremia.

In some cases the patients die from the diphtheria toxemia alone; but in most of the fatal cases one or the other of the complications is the direct cause of death. Most important of these is the pneumonia. Although most often seen in laryngeal cases, pneumonia is a common sequela of diphtheria, either nasal or pharyngeal. The onset of the bronchopneumonia is usually marked by a decided rise in the temperature, a quickened respiration, and some cough. Not till the pneumonia has advanced to the consolidation of large areas do definite physical signs attest its presence. Usually we hear more or less numerous fine crackling râles over one or both chests posteriorly. Later there may be scattered areas of dullness, with bronchial voice and breathing. For evidence of the onset we must depend upon the rational rather than the physical signs. The development of pneumonia is always a grave and often a fatal complication. In but few fatal cases do we fail to find a more or less extensive involvement of the lungs, and in the greater number it plays an important part in the unhappy outcome.

If the view at present generally held, that the complicating pneumonia is dependent upon the action of streptococci or pneumococci and not upon that of the diphtheria bacillus itself, and, therefore, antitoxin can only indirectly affect its onset or its violence, be true, then the problem of further reducing the mortality of diphtheria must depend upon the solution of the prevention and treatment of this complication. At present it is of importance to watch for signs of its onset and to be prepared to take measures to limit its extension and enable the patient to bear the attack. The most malignant cases of diphtheria die within forty-eight hours of the onset of the disease, and even in these we find more or less extensive areas of bronchopneumonia. Most of the fatal cases terminate after five or ten days, the patients being exhausted by the toxemia of the disease or the pneumonia.

In the more favorable cases improvement usually begins about the fourth or fifth day. The change is shown in both the blood and the general condition. In the throat the membrane ceases to extend and begins to separate. The separation begins upon the edge of each patch, the separated portions forming loosened tags in the nose or throat, or the membrane may come away *en masse* in the form of casts of the affected parts. The surface beneath the membrane is at first raw and bleeding, but is usually quickly covered by new epithelium. On the tonsils, however, ulcers are formed, which, healing slowly, leave irregular, depressed areas of cicatricial tissue, giving to the tonsils the excavated appearance so often seen after severe diphtheria. With the separation of the membrane the purulent discharge from the nose and mouth gradually ceases, but a catarrhal secretion may continue for weeks afterward, such catarrhal secretion still containing virulent bacilli.

With the change in the local condition the temperature gradually falls, the pulse improves, the glandular swellings subside, the dullness or stupor disappears, and at the end of the second or third week the patient is convalescent. The patients are usually left very anemic, and the return to health is likely to be slow.

From time to time we see cases in which the formation of membrane continues for two or three weeks, the course of the disease is protracted, and recovery correspondingly delayed. In other cases the bronchopneumonia persists long after the disappearance of all evidences of the diphtheria, and may either cause death from exhaustion or may slowly resolve.

3. Cases of Mixed Infection, or Septic Diphtheria.—Under this head are grouped those cases in which bacteriological investigation shows the presence of the diphtheria bacillus, together with other pathogenic bacteria, usually streptococci, in some cases pneumococci, and in which these additional organisms seem to exert a definite influence upon the course of the disease. Most of these cases are fatal, and in post-mortem examinations systemic infection with streptococci or pneumococci is said to be found. The appearance of the membrane in these cases does not differ essentially from that seen in the severer forms of infection with the diphtheria bacillus alone. It may be white, yellow, gray, or olive colored, or where hemorrhages accompany the inflammatory process more or less black. The membrane is usually extensive, covering the tonsils, pharynx, fauces, and uvula. The swelling of the affected parts is usually very marked, the edema being pronounced, the tonsils often so filling the throat as to preclude examination of the pharynx and giving rise to dysphagia and dyspnea. There is the same mucopurulent or bloody discharge from the nose and mouth; the nares are obstructed and the patients often breathe only through the mouth. A peculiar sickening, sweetish fetor is characteristic. The lymphatic nodes and cellular tissues of the neck are most commonly swelled and indurated, the process in many cases leading on to suppuration and occasionally to gangrene. The pressure upon the veins of the neck may produce congestion of the head and swelling of the face. The swelled, dusky features, with the sanious discharge from nose and mouth, is characteristic and impressive.

The constitutional symptoms are those of a profound septicemia. The temperature often runs as high as 104° or 106° F. (40° or 41.1° C.), but may not be remarkable. The pulse is rapid, feeble, and compressible. With the feebleness of the pulse, the extremities may be cold and pale, in marked contrast to the dusky face.

Vomiting and diarrhea are common, and may be persistent. The urine contains considerable albumin and casts, and in some cases blood. The quantity may be diminished; suppression may occur and cause death from uremia. Edema of feet or hands may be seen. The liver and spleen may both be enlarged. The cerebral symptoms are marked. The patients are usually dull and stupid, indifferent to their condition or surroundings, but at times they are delirious and extremely restless, tossing continually from side to side or crying out as though in pain. Bronchopneumonia is very common and usually hastens death. At any time during the course of the disease the larynx may be involved by extension. The cases, as a rule, terminate fatally within a week, sometimes within forty-eight hours. Rapid failure in the strength of the heart marks the fatal progress of the disease, and the end may be brought about by sudden and unexpected syncope. If they survive the first violence of the infection, these cases are especially liable to complications attributed to the pathogenic action of the streptococci, such as suppuration of the cervical lymph-nodes and cellular tissues, bronchopneumonia, and nephritis.

4. **Laryngeal Diphtheria.**—The clinical picture of laryngeal diphtheria does not present such variety as is seen in diphtheria of the pharynx and tonsils. The local effects, due to the anatomical form of structure of the larynx and its physiological function, predominate over the constitutional symptoms. The mucous membrane of the larynx possesses but little absorptive power; so that as long as the diphtheritic process is limited to the larynx the toxemia is slight.

From what has been already said it is evident that we may have laryngeal diphtheria:—

1. As a primary affection.

2. As an extension of a process beginning either in the nose or the throat.

It may also occur:—

3. As a complication of other infectious diseases, especially measles or scarlet fever. In the latter relation it is less common than the pseudomembranous laryngitis produced by the action of staphylococci or streptococci (pseudodiphtheria), and occurring as a complication it presents itself in one of the two preceding ways, either primarily or secondarily to diphtheria of the nose or throat.

Diphtheria of the larynx begins gradually with a hoarse cough and voice, and perhaps a slight stridor with inspiration. The temperature is usually low,—99° to 101° F. (37.2° to 38.3° C.),—and the child does not appear very sick. The early stages are not to be clinically distinguished from acute catarrhal laryngitis, except that the onset of the latter is usually more abrupt and the temperature higher—102° to 103° F. (38.9° to 39.4° C.). The course of diphthertic laryngitis has the following rather characteristic sequence of symptoms: Croupy cough, croupy inspiration, aphonia, stridulous expiration, suprasternal and infrasternal recessions, restlessness and jactitation, and cyanosis. The cough becomes more and more hoarse; the voice, at first hoarse, fails steadily until the aphonia becomes complete; the stridor, at first only affecting inspiration, shows itself with expiration and becomes louder. With the increase in the local symptoms the temperature may continue low or may mount step by step to 104° F. (40° C.) or more. At the end of the first or second day, sometimes within twelve hours, the symptoms of laryngeal stenosis become well developed. The voice is sunk to a whisper or lost altogether, the cough is very hoarse and short (tight), there is loud stridor with both inspiration and expiration, and every effort to fill the chest grows slower and more labored. With each inspiration there is more or less marked depression of the suprasternal and supraclavicular spaces and the epigastrium. The finger-tips are blue, the lips livid, the face pale, the forehead and perhaps the whole body bathed in perspiration as the child struggles to overcome the increasing obstruction to respiration. The perfect clearness of mind is in marked contrast to the dullness or stupor usually seen in severe types of diphtheria elsewhere. As the agony increases, the child sits up, supporting the shoulders by the arms to give free play to all the accessory muscles of respiration, or, wild with fear, throws himself from side to side or up and down in a vain effort to shake off the tightening grip upon his larynx. It cannot be too strongly laid down that the laryngeal stenosis seen in these cases is largely the result of spasm of the laryngeal muscles excited reflexly by the inflammatory process and in small part the result of mechanical obstruction by membrane or the swelling and edema that accompany it. Often we see fatal cases of laryngeal diphtheria in which the stenosis has required operative treatment, showing only a fine granular membrane, the lumen of the larynx still wide. How much swelling and edema may disappear at the time of death we cannot say, but certainly membrane alone rarely obstructs the larynx. This view is strengthened by the common experience that any excitement greatly intensifies the severity of the stenosis. A child may sleep quite comfortably though breathing stridulously and with some labor; waken it and with the first frightened cry the larynx closes as though in a vice, and, unless the child be quickly quieted, operative relief will soon be required. This point is dwelt upon at such length for the purpose of enforcing its consideration in treatment. Quiet will do a great deal in controlling advancing stenosis. Vomiting will, for a time, relax the spasm, but in true diphtheria the stenosis rapidly returns. At any time the severity of the stenosis may relax, the symptoms all gradually subside, and the patient go on to make a good recovery, but, unless relieved by treatment, the cases usually end in death by suffocation. In such a case the cyanosis deepens, the respiration becomes more and more labored, the violent struggles for air cease, the patients sink into stupor, convulsions develop, and death soon follows.

Such an outcome is most common in infants, who usually succumb in from twenty-four to forty-eight hours from the onset. In other cases the course is slower; the disease reaches its height in from two to three days and terminates within a week.

Bronchopneumonia is a common complication of laryngeal diphtheria. It may develop as the result of direct extension of the membrane from the larynx to the trachea and bronchi, or it may result from the inspiration of the inflammatory exudate containing pathogenic bacteria. The mode of its development cannot be clinically determined. Its presence is indicated by heightened temperature, more rapid respiration, greater cyanosis, usually numerous coarse or subcrepitant râles over both chests posteriorly, and more marked prostration. It makes the prognosis much more grave in any case and frequently causes death when the stenosis has been relieved by operation. It was one of the late Dr. O'Dwyer's observations that, in descending diphtheria, when the membrane passed from the trachea into the median bronchi, this invasion of a new territory was marked by a rapid rise of temperature, which, in turn, was soon followed by developing pneumonia.

Case of diphtheria in a boy aged 6½ years in which a thick gush of blood

> poured out of the tracheotomy wound, death taking place in eight seconds. At the autopsy there were found: erosion of the common carotid at its origin by an abscess cavity which communicated with the trachea; deep ulceration of larynx, superficial ulceration of trachea, aspiration of blood and pus into lungs; perforation of subpleural abscess of left upper lobe with circumscribed fibrinopurulent pleurisy; subacute nephritis, edema, and cloudy swelling of liver. Erosion of the cervical vessels has been recorded in scarlet fever, but never before in diphtheria. O. Lukinger (Brit. Jour. Child. Dis., Aug., 1911).

When laryngeal diphtheria develops secondarily to diphtheria of the nose or throat, or as a complication of the infectious diseases, the symptoms above described are superadded to those of the original affection, and the patient is all the less likely to survive.

COMPLICATIONS AND SEQUELÆ.—Otitis media is an occasional complication of diphtheria. It is developed by direct extension of the inflammatory process through the Eustachian tubes and belongs to cases in which the rhinopharynx is involved in the diphtheritic process.

In some cases the ear affection is of the severest type and there is considerable destruction of the drum membrane. It may even result in gangrene.

> Nine cases of gangrene of parts distant to throat, such as a limb, following diphtheria, are recorded in the literature. It was connected with a definite vascular lesion. In 7 cases the lesion was a definite embolism; in 1 it is termed Raynaud's disease, and in 2 the origin is obscure. In 6 out of the 9 cases the leg was affected; in 1 there were, in addition, widespread gangrenous lesions. In 2 other cases there was a widespread necrotic affection. Ransome and Corner (Lancet, Jan. 14, 1911).

Pneumonia, as stated, is the most frequent and dangerous complication. It is most common in laryngeal diphtheria, but may follow any form of the disease. It is attributed to the action of the pyogenic cocci, especially the streptococci and the pneumococcus, though Stephens and Kanthack, Wright, More, and others have demonstrated the presence of the diphtheria bacillus in the lungs.

> Case of a girl, aged 4 years, who progressed favorably until after a fortnight's residence in hospital, when she became moderately feverish and very restless, and presented signs and symptoms pointing to pulmonary trouble. Alteration of the respiratory murmur was made out over the right upper lobe, though from the increasing restlessness examination was difficult. The child grew very rapidly worse, with increasing lividity, restlessness, and respiratory embarrassment. Death took place within twenty-four hours of the first appearance of symptoms. At post-mortem examination a large infarction implicating the upper right lobe was found. D. Stewart (Lancet, March 30, 1912).

The affection takes the form of bronchopneumonia and is commonly met with in the lower lobes, but may be seen in any part of the lungs. The areas are scattered and separate or may merge into one another till considerable portions of both lungs are consolidated. This complication usually develops at the height of the disease, but may occur at the very beginning, within the first twenty-four hours, or may arise during convalescence after the throat is clear. Its onset is marked by increased temperature, disturbance of the respiration-pulse ratio,—namely, from a relation of 1 to 4 to 1 to 3,—greater prostration, and the signs of a diffuse bronchitis; only when considerable areas are involved do we obtain the signs of consolidation.

Lobar pneumonia may occur (0.7 per cent. of cases—Rolleston) and run the clinical course of this disease.

> Observations made on 1000 consecutive cases of diphtheria under the writer's care at the Grove Hospital (London) during the past four years. Lobar pneumonia occurred in only 7 cases (0.7 per cent.). All the patients were children, their ages ranging from about 2 years to 7 years. The more favorable prognosis of lobar pneumonia as compared with bronchopneumonia is illustrated in the writer's cases by the fact that whereas none of the 7 cases proved fatal, only 3 of the 15 cases of bronchopneumonia among the 1000 cases of diphtheria recovered—a mortality of 80 per cent. J. D. Rolleston (Brit. Jour. Children's Dis., Dec., 1906).
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> In 287 cases of fatal diphtheria only about 25 per cent. succumbed to general diphtheritic intoxication, and a little less than 25 per cent. to tardy paralysis. All the others—more than 50 per cent.—died in consequence of pulmonary lesions. The latter were the cause of death in all the infants and in 83 of the 139 cases in children between 1 and 3, and in 16 of the 85 cases in children from 4 to 10, which included also 33 cases of fatal tardy paralysis. The 17 fatal cases of diphtheria in patients over 10 included 9 deaths from early general intoxication, 3 from tardy paralysis, and 3 from tardy sepsis. He remarks that far too little attention has been paid hitherto to secondary infection in diphtheria. Fischer (Hygiea, vol. lxviii, No. 9, 1906).

Pleurisy is rarely met with. Empyema may develop, especially in septic cases. Emphysema is frequently seen in laryngeal cases; it may be interstitial and may extend to the cellular tissues of the neck, but is commonly vesicular.

The heart is more seriously affected in diphtheria than in any other acute infectious disease, and many of the fatal cases are due to rapid or sudden heart-failure. It follows tonsillar or pharyngeal diphtheria frequently, and is rare after other forms. Goodall, in a recent study of these cases, gives three types of the affection:—

1. Heart-failure while the exudate is still present in the throat and before other symptoms of paralysis present themselves. It is then due to the direct action of the diphtheria toxins upon the nerve mechanism of the heart.

2. Heart-failure after the disappearance of membrane, but during the time of other symptoms of paralysis, when it may be due either to disturbed innervation or to fatty changes in the heart muscle, such as are met with in other fevers.

3. Heart-failure during convalescence, some time after the disappearance of membrane; it is then probably caused by degeneration of the heart muscle or of the pneumogastric nerve (neuritis).

Whether occurring early or late in the disease, the symptoms of involvement of the heart are, in general, the same: the pulse becomes either more rapid or more often slower; it may be intermittent or irregular; in any case it is much weaker. The patients are greatly prostrated, may refuse food, and may vomit repeatedly. The surface of the face and extremities may be pale and cold, or there may be dyspnea without cyanosis. There may be some precordial distress. After continuing in this condition for hours or days the patients may rally, the heart gradually resumes its normal action, the symptoms disappear, and recovery ensues. More often the alarming symptoms grow worse and the patients succumb to the cardiac weakness. Death may be caused by sudden syncope induced by slight exertion or excitement. In some of the cases the patients are regarded as thoroughly convalescent, and may be up and about when sudden and unforeseen paralysis of the heart results in instant death. The cardiac affection, while most often seen after severe diphtheria, may be a sequela of the mildest cases. Severe and persistent vomiting during convalescence is always suggestive of impending heart-failure. Hemorrhages into the skin or from mucous membranes may be met with during the height of the disease. They are most frequent from the nose and may be so severe as to require plugging of the posterior nares. They may occur from other mucous membranes: the stomach, intestines, or rarely the bladder. In the skin the hemorrhage may give rise to petechiæ or may infiltrate considerable areas.

The petechiæ are most often seen upon the abdomen and lower extremities, but may occur upon any part of the body. They are caused by changes in either the blood or the vessels or both, and are usually seen in the severer types of toxemia. The hemorrhages are in some cases sufficient to seriously exhaust the patient, and may even cause death. Exanthems, which may be morbilliform, scarlatinal, or urticarial, may appear, unassociated with the use of serum.

> Four cases of a phlegmonous skin affection, from which the diphtheria bacillus was obtained in pure culture. None of the patients had faucial diphtheria. Ehrhardt (Münch. med. Woch., Bd. liv, Nu. 24-25, 1907).

Thrombosis and embolism are among the rarer complications of diphtheria. They may affect the extremities, giving rise to the usual symptoms: sudden pain, numbness, and coldness of the limbs, followed by paralysis, edema, and even gangrene. Some of the cases of cardiac paralysis may be caused by thrombosis or embolism of the vessels of the heart. Affecting the cerebral arteries, thrombosis, embolism, or hemorrhage may give rise to hemiplegia.

In very rare cases the stomach may be involved in the diphtheritic process; but, apart from such involvement, gastric symptoms are common.

> Case of a boy, aged 2 years and 4 months, who was admitted to hospital on the eleventh day of disease and died in seven hours. At the *post mortem*, among other findings, the middle third of the esophagus presented some infection of the mucosa, and in the lower third "were two longitudinal areas of necrosis, 3.5 c.m. each in length, coalescing below, where each measured 2.2 c.m. in width, and stopping just short of the lower end of the esophagus. No diphtheritic membrane was left, but direct smears and cultures showed numerous diphtheria bacilli." It is rare to find the esophagus involved; the writer found that 22 cases had been recorded since the discovery of the bacillus. J. D. Rolleston (Brit. Jour. of Dis. of Children, Jan., 1912).

Persistent vomiting is a frequent and grave occurrence in severe cases. It may be due to the fever and toxemia, or to nephritis, or to heart-failure.

> Besides the familiar complications such as cardiac failure, paralysis of the diaphragm, suppression of urine, bronchopneumonia, and certain nervous sequelæ, others may occur. The first of these is enlargement of the liver, usually associated with cardiac failure, and due to distention of the liver capillaries with blood. If recovery occurs the liver usually returns to its normal size. Disease of the arteries is also a complication, yellow patches being found in the aorta, and in the mitral valve, and nodules of varying size in the smaller arteries, especially in those of the brain. They are supposed to be due to septic micro-organisms, which are associated with the diphtheria toxins. Interlobular emphysema may occur, the air which has escaped from the alveoli of the lung appearing beneath the pleura.

It may result in pneumothorax. Clubbing of the fingers is a rare complication, and has been occasionally seen in children with whom gangrene of the lung has developed. T. Fisher (Pract., Oct., 1907).

Diarrhea is often met with during the height of the disease, and may persist for some time after the diphtheria itself is improved. It may be due to enterocolitis or may be dependent upon the constitutional condition, especially in the septic cases. The local lesions are not severe and have no direct relation to the diphtheritic process. As already noted, hemorrhages may occur from either stomach or intestine in rare cases.

Case of abdominal diphtheria. There was severe abdominal pain and vomiting of bile-stained fluid. Both recti muscles were rigid and contracted spasmodically, equally on both sides. There was tenderness all over the abdomen, but slightly more localized in the epigastrium. The patient was very much prostrated. Leucocytes numbered 14,000. The second day the temperature and pulse were slightly elevated. A suspicion of diphtheria was aroused by the low fever and prostration resembling that of several other diphtheria patients in the hospital at the same time. Patient's throat examination was negative clinically, but the writer had found diphtheria organisms in the throats of several persons of normal appearance. Hence cultures were made from the throat of this man. On the third day, a twelve-hour culture showed abundant diphtheria organisms. Bowels, which were very constipated, were moved with calomel and enema. The movements had the foul odor characteristic of diphtheria. **Antitoxin** was prescribed, 4000 units every six hours. On the fourth day the patient was improved; mind was clearer, and he had less pain. There was also decreased rigidity of the recti. By the eleventh day all symptoms had disappeared. F. Schmitter (Military Surgeon, Nov., 1910).

The kidneys are more or less affected in all severe cases of diphtheria. The lesion may be an acute degeneration, marked by more or less albumin in the urine, or acute exudative nephritis with albumin and casts, but without dropsy or uremic symptoms. Very rarely an acute diffuse nephritis with diminished urine containing albumin and casts, or suppression of the urine, dropsy, and uremia may be seen.

The albuminuria usually comes on during the height of the disease, continues for a time, and disappears rapidly with improvement in the local symptoms. Only in the rare cases in which acute diffuse nephritis develops are the renal complications likely to persist. Marked albuminuria is always an evidence of a grave infection, while not of itself a serious complication. It is most common in the septic cases, and belongs distinctly to pharyngeal, or tonsillar, diphtheria. In very rare cases there may be hemorrhages from the kidneys.

To 41 cases of puerperal infection with diphtheria bacilli on record, the writer adds one. The false membranes develop at the site of lacerations or other lesions. Edema of the external genitals is an important symptom when present, as in his case, and swelling of the regional lymph-nodes was pronounced in a number of cases, generally bilateral. This enlargement of the glands was an early sign. Paralysis of the sphincters was observed in some cases. The fever usually corresponds with the severity of the membrane production, but in 2 cases the temperature remained normal. In some the fever was the first sign. Prostration and somnolency were extreme in some cases; headache was another symptom. Besides these phenomena, there was, in the writer's case, great difficulty in breathing, but no wheezing or croupiness. Bourret (Obstétrique, October, 1911).

Mention has already been made of the fact that, pathologically and experimentally, the most characteristic lesion of diphtheria is that affecting the nervous system and giving rise to paralysis of various groups of muscles. Clinically, paralysis is infrequent, but in its distribution, type, and course none the less characteristic. In 2448 cases collected by Sanné paralysis was noted in 11 per cent.; in a series of 1000 cases reported by Lennox Browne in 14 per cent.; in 1071 cases belonging to preantitoxin days studied by Goodall, after deducting a mortality of 33.8 per cent., he says he observed paralysis in 125 of the 709 survivors,—17.6 per cent. of the latter number, or 11.7 per cent. of the whole number; in 3384 cases treated by antitoxin comprised in the Report of American Pediatric Society paralysis was met with in 328 cases,—9.7 per cent. of the whole number. Of the 2934 cases that recovered, 276—or 9.4 per cent.—showed paralysis, while, of the 450 fatal cases, paralysis was observed in 52, or 11.4 per cent. Simply taking the totals of these figures without relation to the question of treatment, we have 852 cases of paralysis occurring among 7903 cases, or in 10.7 per cent.

Paralysis usually complicates the severer cases of pharyngeal diphtheria, but may be seen after milder forms, and it has even been reported as following affections of the throat so mild as to have attracted little or no attention.

The time of the onset of paralytic symptoms varies greatly in different cases. It may occur at the height of the disease in the latter days of the first week or the beginning of the second, but is usually seen some time after the throat is altogether clear during the third or fourth week of the disease, and may occur as late as the tenth week after the onset. In the cases reported by Goodall the paralysis was observed from the seventh to the forty-ninth day.

In 171 cases of diphtheritic paralysis collected by Ross the following distribution was observed: Palate affected in 128; eyes in 77, in 54 of which the muscles of accommodation suffered; lower extremities in 113; upper extremities in 60; trunk or neck in 58; muscles of respiration, 33. Of the 328 cases reported to the American Pediatric Society the distribution was specified in 187.

Of this number in 120 involved the throat (palate, pharynx, and larynx); in 14 the extremities; in 11 the eyes; in 32 the heart; in 1 the muscles of respiration; in 1 the sternomastoid, and in 8 the paralysis was general.

In the series published by Goodall, the palate alone was first affected in 66 per cent. of the 125 cases, and in combination with other muscles it was involved in 12 per cent. more. In a little over one-half of the cases the paralysis was limited, and in 12 per cent. it was generalized. The affection of the throat is, therefore, much the most common. It may occur alone or be followed by paralysis of other parts: the eye, the extremities, the trunk, or neck. In some cases it precedes the cardiac paralysis, but, as a rule, this most grave form of diphtheritic paralysis appears unannounced. Absence of the patellar reflexes is observed in most cases of diphtheritic paralysis, even when there is no loss of power or sensation in the lower extremities, and is regarded as a sign of the probable appearance of paralysis elsewhere.

Of 1313 patients seen by the writer 85, or about 6 per cent., became paralyzed. Of these 85 patients, 65, or 77 per cent., recovered and 20 to 23 per cent. died.

In no one case could death be attributed solely or directly to paralysis, although in all cases it was contributory. In 10 of the cases that terminated fatally the disease was of the malignant type, while in the others it was of a severe character. Eight had nasal implication, 7 a combination of faucial and laryngeal diphtheria with tracheotomy in three instances, and 27 had greatly enlarged cervical glands. Of the latter, 2 went on to suppuration. Of the 85 patients, 53, or almost two-thirds had paralysis of the palate alone; 15 of the eyes and palate; 3 of the eyes alone (strabismus). Of the 15 who were afflicted with paralysis of the eyes and palate combined, 3 had paralysis of accommodation as well as strabismus. Paralysis of the ocular muscles alone is uncommon, and only 2 of the 68 patients recorded were affected in that way. Of the 12 patients noted as having intercostal and cardiac paralysis, 9 died and 3 recovered, the main symptoms being great difficulty in inspiration with marked feebleness and irregularity of the heart. In the one case in which the lower limbs only were affected the loss of power lasted only for a few days. The average duration of the paralysis was eighteen days. The urine varied greatly as regards albumin. Of the 85 patients, 27 had a large quantity of albumin in the urine, 18 had a moderate quantity, 17 a mere trace and 23 no albumin in the urine at all. With one exception there was a large quantity of albumin in the urine of all the fatal cases. A. Love (Jour. Amer. Med. Assoc. from Glasgow Med. Jour., Oct., 1911).

In most of the throat cases the uvula and soft palate alone are involved. Nasal voice and regurgitation of fluid through the nose evidence the loss of power in these parts, and upon inspection we see the uvula hanging straight downward, relaxed, and motionless upon the back of the tongue. Sensation as well as motion is gone, and there will be no response to irritation. If the pharyngeal muscles are involved, there is difficulty in swallowing, and, if the larynx suffers, there will be aphonia and severe coughing upon attempt at swallowing anything by reason of the entrance of food or drink into the imperfectly closed organ. The latter class of cases is very likely to prove fatal through the development of pneumonia from the inspiration of foreign material. In the extremities—arms, legs, or neck—we see more or less complete loss of power and sensation. The paralysis may not, however, be generalized in these parts, but appears at times to attack only the muscles supplied by a particular nerve-trunk, or even a branch of a main nerve. The paralysis may be so extensive as to render the patient perfectly helpless. When the trunk is involved, the gravest danger arises from implication of the muscles of respiration. Usually the diaphragm is first involved, but the intercostals may suffer. If the diaphragm is paralyzed, the respiration is entirely thoracic; if the intercostals, then the diaphragm alone must do the work. Either affection is characterized by attacks of urgent dyspnea, with cyanosis. The mind being perfectly clear and respiration maintained only by the greatest effort on the part of the victim, the distress is often terrible. The danger of suffocation is imminent. Such an attack may pass off and there be no return; but more often they recur in a short time. The patient may remain in this condition for several days, before death finally ends the struggle.

Few of these cases recover: only 8 in 33 of Ross's series. At any time there may be involvement of the pneumogastric nerves as well as the phrenic, the new invasion declaring itself by attacks of abdominal pain, vomiting, and feeble and slow or irregular pulse. At other times the heart may continue to act normally despite the respiratory distress.

We have already spoken of the purely cardiac type of this affection, for it is impossible on clinical grounds to separate from one another the cardiac failure due to changes in the myocardium from that produced by involvement of the pneumogastric or other cardiac nerves by the neuritis. Furthermore, the two conditions are often associated. It may be well again to point out the suddenness with which cardiac paralysis may occur by quoting from the Report of the American Pediatric Society the following paragraph: "Observations of some of the individual cases are interesting, particularly those of cardiac paralysis. It is twice stated that the child had gotten up and walked out of the house, where it was found dead.

"Twice death occurred after sitting up suddenly; once, on jumping from one bed to another. One patient of 20 years got up contrary to orders and died soon afterward. Another patient was apparently well, until he indulged in a large quantity of cake and candy, soon after which cardiac symptoms developed and he died shortly."

When the eyes are affected there is indistinctness of vision, usually resulting in inability to read, caused by paralysis of the muscles of accommodation. The pupils may be dilated or sluggish in action from involvement of the sphincter iridis. Strabismus or ptosis from paralysis of the extrinsic muscles of the eyes is rarely seen.

Facial and glossal paralyses have both been reported, and in some of the severest types of general paralysis the sphincters of the bladder and rectum are said to have been involved.

If the case does not result fatally, either directly from the paralysis or from the diphtheria itself or other complications, the paralysis will surely recover. In none of the cases observed by Goodall was the paralysis permanent. The time required depends upon the degree and extent of the paralysis. Those in which the throat alone is affected usually recover completely within a week or two. Cases of multiple or generalized paralysis may require three or four months to regain normal power.

> Relapses occur in a little more than 1 per cent. of all cases of diphtheria. They are less frequent than late tonsillitis in convalescence from diphtheria. They do not occur before the third week. The frequency of serum rashes after reinjection is much greater, their appearance is earlier and their phenomena are more intense than usual. Relapses must be distinguished from angina redux, scarlet fever and late tonsillitis. They are usually milder than the primary attack. Comparatively small doses of **antitoxin** should be employed in the treatment of relapses. Rolleston (Brit. Jour. of Dis. of Children, Aug., 1907).

DIFFERENTIAL DIAGNOSIS.—The bacteriological investigations inspired by the identification of the Klebs-Löffler bacillus have greatly simplified the question of the relationship of the various pseudomembranous inflammations.

We now know definitely that there are but two great types: the one termed pseudodiphtheria, produced by streptococci or staphylococci and belonging to the acute infectious diseases,—measles or scarlet fever,—and true diphtheria, produced by the specific bacillus, and usually a primary and independent affection.

> Research on the way in which the skin of children reacts to inoculation of bacterial toxins. A positive reaction was obtained in 38 per cent. of the 448 children inoculated with diphtheria toxin, but only in 4 of the 72 inoculated

> with typhoid toxin. The tuberculin skin test was applied to the arm at the same time with the diphtheria toxin in 156 children, but there was no concordance between the results. The most pronounced reaction to the diphtheria toxin was obtained in the group of 47 per cent. responding positively among the 168 scarlet-fever patients tested. This confirms the writer's assumption that scarlet fever and febrile sore throat are allied affections. Szontagh (Archiv f. Kinderheilkunde, Bd. lviii, Nu. 4-6, 1912).

On the other hand, these investigations have added complexity to the problem of diagnosis of throat affections by showing the presence of the specific bacilli of diphtheria in many cases of sore throat free from membrane and previously passed over as simply "catarrhal" sore throat, and also in many of the cases of a fairly definite clinical type, formerly classified as follicular tonsillitis.

> The very slightest excuse should be sufficient for the diagnosis of diphtheria in a child. Even so slight a sign as dryness or a parched appearance of the external nares in a child who seems poorly nourished is sufficient to indicate, in most cases, that diphtheria toxin is being manufactured, probably in the nasopharynx. Diphtheria antitoxin never does any harm to a child, and it will assist in curing illness due to some disturbance in the throat or nasopharynx, even if that illness is not actually due to diphtheria. Rhodes (Brit. Med. Jour., Feb. 17, 1906).

> Primary diphtheria of the larynx occurs more frequently than is usually recognized. It should be suspected when hoarseness in a child is constantly increasing and stenosis and aphonia develop in from one to three days. Primary diphtheria of the nose also is often overlooked. Every febrile coryza with enlargement of the glands and impairment of the general health is suspicious, especially when the discharge is thin and purulent, with traces of blood. The nasal variety may run a very mild, protracted course, and its true nature may not be suspected until contacts develop diphtheria of a severer type. Infants are exceptionally prone to primary and isolated diphtheria of the nose. E. Freer (Deut. med. Woch., April 4, 1912).

In the shifting of the lines that has followed these revelations a considerable degree of mental confusion has been engendered and an uncertainty fostered that has led many to lose all faith in the results of clinical observations. If it is necessary to rearrange the lines of classification somewhat, it is not required that we abandon all our former conceptions or no longer trust to careful observation. In the great majority of cases thorough examination and careful consideration of all the factors concerned will enable one to reach a positive diagnosis without awaiting the results of a bacteriological examination, although the latter should always be employed if possible. For the sake of clearness we shall follow the order adopted in the description of clinical symptoms.

Nasal Cases.—The only cases that are difficult of diagnosis are those of primary nasal diphtheria. The thin, irritating, mucopurulent discharge, often brownish from the presence of blood, is quite different from the abundant, ropy mucus seen in simple catarrhal inflammation. Excoriation of the nares and eczema of the upper lip produced by the discharge are suggestive of diphtheria. Careful inspection may show the presence of more or less white or grayish-white exudate on the mucous membrane, in which case the diagnosis of diphtheria may be safely advanced. Furthermore, the diphtheritic cases are usually accompanied by some slight rise of temperature, anorexia, and a distinct degree of constitutional depression not seen in cases of simple inflammation. In diphtheritic rhinitis the lymphatic glands are usually enlarged, while in the simple forms of rhinitis glandular enlargement is infrequent. Finally, these cases are much more often seen in institutions where the children are more or less constantly exposed to diphtheritic infection than in private or dispensary practice.

We are less careful in diagnosis now than in the preantitoxin period. Primary nasal diphtheria differs from ordinary faucial diphtheria in being a subacute or chronic process, and of slight toxicity; but these cases harbor the bacilli longer than those of the faucial type, so that isolation should be prolonged. There are two types. In one there is a formation of false membrane, sometimes completely filling one or both nasal fossæ with casts, and a watery, acrid, mucopurulent discharge. The other is merely a diphtheritic inflammation of the mucosa with a copious watery discharge of acid mucopus. The fibrinous type is commoner in older children, the catarrhal type in infants. There is a tendency to reinfection and relapse. Hubbard (Annals of Otol., Rhin., and Laryn., March, 1908).

Nasal diphtheria in infants, in a large percentage of cases, is mistaken during the first days and even the first weeks of the disease for the ordinary "snuffles" or coryza. Notwithstanding the fact that this condition is frequent in infancy, and that the child's appearance is characteristic to the experienced eye, the true diagnosis is often not made until a rapid loss of weight and strength, a diphtheritic otitis media, or an absolute occlusion of the nasal passages make their appearance. It is, therefore, important to make a diagnosis immediately by direct nasal examination, before receiving the bacteriological report. It is desirable to be able to diagnosticate the bacilli carriers from those ill with the disease. Direct nasal inspection is remarkably easy in the newborn. In the recumbent position, with the child's nostrils separated by a bent hairpin or an open speculum, a good view of the nasal passages is obtained. If the child is not crying, pressing backard the tip of the nose is often sufficient. Blochmann (Berl. klin. Woch., Bd. xlvii,, S. 2008, 1910).

Pharyngeal, or Tonsillar, Cases.—These often present difficulties in diagnosis, but a full consideration of all the factors in any case will usually lead to a correct judgment. The most difficult cases are the milder ones, where there is little or no membrane and the constitutional symptoms are slight. The question of exposure should be considered in every case. Children gathered in hospitals, or asylums, or attending schools are especially exposed to diphtheritic infection, and in them any form of sore throat may justly be looked upon with suspicion. So far as the catarrhal form of diphtheria is concerned, even with a history of exposure, there is no way of making a diagnosis of diphtheria in the early stages except by bacteriological cultures. The after-course of some of these cases—in which we may see invasion of the larynx, bronchopneumonia, nephritis, or paralysis—may show them to have been diphtheria when no suspicion has previously been entertained.

Two cases of pseudophlegmonous angina of diphtheritic origin were observed by the writers. They found 25 on record, with 5 fatalities. This form of diphtheritic sore throat is most common between the ages of 15 and 30; children seldom present it. In another case they encountered a phlegmonous angina which simulated true diphtheria, although of non-diphtheritic origin. In a certain number of cases in the literature the two affections were associated. Diphtheria antitoxin should be injected without waiting to ascertain whether the diphtheria bacilli are to be incriminated or not. Roger and Margarot (Arch. gén. de méd., May, 1909).

When diphtheritic membrane is present in the throat, it usually presents certain definite characters. It begins as a thin, translucent deposit upon one or both tonsils. Gradually or rapidly it becomes thicker, and assumes a white, gray or grayish-green, brown, or—in malignant cases—black color, and extends peripherally to cover a larger and larger area. It is firmly attached to the mucous membrane or underlying tissues and cannot be easily rubbed off. If removed by force, a raw, bleeding surface is left, and in a very short time the membrane is reproduced in its original or even a greater extent. Beginning upon the tonsils, the membrane rapidly extends to other parts: the lateral walls of the pharynx, the fauces, or uvula. Upon any of these parts the membrane presents the same characters as at the original site. This extension of the membrane is most characteristic of diphtheria. The only cases in which we are likely to see such extension of a pseudodiphtheritic membrane are the throat inflammations accompanying other infectious diseases, measles, small-pox, and—most of all—scarlet fever. The great majority of the membranous throat affections seen in the early stages of these diseases are produced by the action of streptococci or staphylococci. When a similar process is seen as a late complication of infectious disease, it is more probably true diphtheria.

The early temperature in diphtheria is not usually high; it is, in fact, generally lower than in pseudodiphtheria, with an equal amount of membrane. A high temperature in the beginning is, therefore, an indication that the case is not diphtheria. On the other hand, the prostration is greater in diphtheria than in pseudodiphtheria. The pulse is feebler; the patients look and feel sicker than they do when suffering from pseudodiphtheria. The presence of a nasal discharge of a character described as belonging to nasal diphtheria and marked swelling and tenderness of the cervical lymph-nodes help to distinguish some cases in the early stages. Later we look for the development of the typical complications or sequelæ of diphtheria: invasion of the larynx, bronchopneumonia, albuminuria, or some of the manifold forms of paralysis. The occurrence of any of these processes is usually sufficient to make the diagnosis certain, although it is not impossible that any of them except the paralysis may be seen in cases of pseudodiphtheria. Paralysis subsequent to throat inflammation is seen only in diphtheria. Pseudodiphtheria is, in the great majority of cases, a milder disease and of shorter course than diphtheria. As already remarked, the primary throat inflammation of scarlet fever most closely resembles true diphtheria. In fact, in every case where diphtheria is suspected, the possibility of scarlet fever must be borne in mind and examination made for the eruption. Oftentimes it will be found at the very first examination; at any rate, a brief delay will suffice to determine the question, as the eruption of scarlet fever so quickly follows the initial symptoms. It may even happen that the throat symptoms of measles may simulate diphtheria, and especially if the eruption be delayed for a number of days. Here, however, there is rarely any membrane at all, and the presence of conjunctivitis, with the simple mucous discharges from nose and throat, should be sufficient to prevent mistake.

After tonsillotomy there is a fibrinous deposit on the stumps of the tonsils, but the absence of constitutional disturbances, and, above all, the history, will prevent confusion with diphtheria.

The form of pharyngitis described by Vincent often gives rise to the appearance of a membrane which may resemble that seen in diphtheria. The deposit may be on one or both tonsils and may spread to the pillars of the fauces and to the posterior pharyngeal wall. This is not a true membrane, such as occurs in diphtheria, but is merely a necrosis of the surface epithelium. In Vincent's angina there is usually less prostration than in diphtheria, and the bacteriological findings in the former of the *Bacillus fusiformis* and *spirilla* and in the latter of the *Bacillus diphtheriæ* will make certain the nature of the disease.

Furthermore, the presence of the spots described by Koplik is diagnostic of measles.

DIFFERENTIAL DIAGNOSIS.

1. Exposure to infection from previous case of diphtheria.	1. No such exposure: arises independently.
2. Greatest liability in early years: first to fifth year.	2. Occurs at any age.
3. Membrane either seen from first upon pharynx, fauces, or uvula, as well as tonsils, or rapidly extends to these parts.	3. Membrane limited to tonsils.
4. Membrane firmly attached to underlying tissues, and not easily rubbed off.	4. Membrane loosely attached and easily removed.
5. If membrane be removed, leaves bleeding surface.	5. Membrane may be removed without such bleeding.
6. If removed, membrane is very rapidly reproduced in an even greater amount.	6. Reproduction of membrane not so rapid or extensive.
7. Discharge from nose thin, irritating, often bloody, and produces eczema of upper lip.	7. Nasal discharge not so common, and is simple mucopurulent.
8. Submaxillary and cervical lymph-nodes swollen and tender.	8. Swelling of lymph-nodes not so marked in primary cases; is regularly met with, however, in throat inflammations of scarlet fever, etc.
9. Membrane may be seen upon buccal mucous membrane, tongue, angles of the mouth, or lips.	9. Not seen upon these parts.
10. Onset gradual; temperature low at beginning.	10. Onset more sudden; temperature higher.
11. Constitutional depression is more marked, the pulse weaker, and children more prostrated.	11. Constitutional symptoms usually in proportion to temperature; more moderate. Pulse rapid, but not weak, and depression not so marked.
12. Course longer: usually five days to a week before marked improvement is seen.	12. Course shorter, except in cases complicating infectious diseases; is usually three or four days.
13. Albuminuria common and severe nephritis frequent.	13. Much rarer.
14. Larynx often involved by extension.	14. Larynx rarely attacked secondarily, except in measles or scarlet fever.
15. Paralysis of more or less extensive groups of muscles may occur, as a complication or sequela.	15. No such paralysis seen.

Laryngeal Cases.—When the laryngitis appears as the extension of a previous process in the nose or throat, except in the case of measles or scarlet fever, we can safely put it down as diphtheritic. The pseudomembranous throat inflammations of measles and scarlet fever often involve the larynx, trachea, and bronchi, although the processes are not usually diphtheritic. In any other case such extension is almost conclusive evidence that we have to do with diphtheria. The greater difficulty is prevented by the primary cases of laryngitis in children. The characteristic feature of diphtheria of the larynx is its progressive, unremitting dyspnea with aphonia. The disease steadily advances to laryngeal stenosis and death from strangulation, unless relieved by treatment. Simple catarrhal, or non-diphtheritic, pseudomembranous laryngitis, on the other hand, usually shows frequent and decided remissions—its crises belonging to the night, the day showing decided remission of all the symptoms. As in the pharyngeal cases, early high temperature belongs rather to the pseudodiphtheria. If laryngeal examination be possible and we can see and determine the character and extent of the membrane in the larynx, we ought to be able to reach a positive diagnosis; but, unfortunately, such examination is not practicable among young children, who furnish the great majority of the cases of acute laryngitis. Of 283 cases of acute laryngitis subjected to bacteriological examination by the New York Board of Health, 229—or 80 per cent.—proved to be true diphtheria; so that in the city, at least, the diagnosis in any such case would incline to diphtheria.

While it is true that, as many authorities maintain, in 95 per cent. of the cases which an expert, after careful consideration, would pronounce diphtheria, cultures will show the presence of the specific bacillus, it must be frankly admitted that there are many cases in which the most careful observation cannot determine positively the question whether a given case is true diphtheria or pseudodiphtheria. Thus, in Scientific Bulletin No. 1, of the New York Board of Health, we find it stated that "Baginsky, in Berlin, found the diphtheria bacillus in 120 out of 154 suspected cases; Martin, in Paris, in 126 out of 200; Park, in New York, in 127 out of 244; Janson, in Switzerland, 63 out of 100, and Morse, of Boston, in 239 out of 400. Thus, from 20 to 50 per cent. of the cases sent to diphtheria hospitals did not have diphtheria." If these figures approximate the truth, it is evident that we cannot trust with safety to clinical observations to determine the specific relation of cases of throat inflammation. On the other hand, the routine use of cultures from all cases of sore throat regularly shows the presence of the diphtheria bacillus in a considerable number of cases in which there were few or none of the features regarded as characteristic of diphtheria, and in which there was, therefore, little or no suspicions of the presence of the specific bacillus.

While so far as the individual case is concerned, it may be remarked that the cases in which the diagnosis is most difficult are the mild cases, those least likely to be attended with grave consequences to the patient himself, the fact should also be recognized that these mild cases are quite as dangerous to others as severe ones, and should, for the sake of the community, be subjected to strict quarantine. It is, therefore, essential to accurate work and proper care, as well as proper prophylaxis, that cultures should be made from all cases of sore throat. In no other way can we stand upon solid ground with relation to treatment, or hope to eventually gain control of the widespread and dangerous infection.

[Scientific Bulletin, No. 1, Health Department of the City of New York, is the source from which the greater part of the material of this section is drawn. W. P. NORTHRUP and DAVID BOVAIRD.]

Methods of Making Bacteriological Examinations.—An immediate microscopic examination of the exudate in cases of suspected diphtheria will often justify a positive diagnosis. A bit of membrane removed from the throat by a swab is smeared upon a cover-glass or slide, dried, fixed by heat, and then stained with Löffler's methylene-blue solution.

With an oil-immersion lens we may then be able to determine the presence of bacilli sufficiently characteristic to warrant a positive diagnosis. The bacilli under such conditions do not have the characteristic features which are presented by cultures upon suitable media. They are much more irregular in size, shape, and staining properties. Positive judgment is, therefore, much more difficult and uncertain. Failure to find the bacilli by this method would in no way prove that the case was not diphtheria. The uncertainties of the method are so pronounced that it is rarely employed.

The best culture medium for routine work is the Löffler blood-serum, coagulated by heat in test-tubes in such a way as to give an extensive slanting surface for inoculation. It is important that the reaction of the medium be neutral or slightly alkaline, for the diphtheria bacillus grows very poorly on acid media. The swabs used in obtaining the infected material from the throat are made by wrapping a small quantity of absorbent cotton about the end of a small steel rod six inches in length. The swabs so made are inserted into test-tubes, which are then plugged with cotton and the whole sterilized by exposure to dry heat at 150° C. for one hour. To make a satisfactory culture a good view of the throat must be obtained and the swab rubbed upon the surface covered by the edge of the membrane, or—in the absence of membrane—upon the inflamed parts. In laryngeal cases where no membrane is visible it usually suffices to make the application of the swab either to the tonsils or as low in the pharynx as possible. In such cases if the first culture fails to show the presence of diphtheria bacilli, it is always well to repeat the process, as second or third culture may show the bacilli previously absent from the accessible parts of the throat. Care must be taken in inoculating the swab not to allow it to touch the tongue or any other part or surface than the one upon which the presence of the bacilli is suspected. Otherwise contaminating bacteria are inoculated upon the culture media and the value of the culture for diagnostic purposes destroyed.

To carry out these directions in young children it is necessary that they be carefully held. The best method is to have the mother or nurse hold the child upon her right side, the child's face turned toward the light and the head resting upon her right shoulder, one of the holder's arms about the patient's legs, the other controlling the arms. The physician can then usually insert a tongue depressor and control the head with one hand, while with the other the swab can be properly directed. With very fractious children it may even be necessary to have a second assistant hold the child's head. Failure to take pains in making a proper application of the swab is accountable for many of the unsatisfactory results obtained from cultures. The swab having been properly inoculated, the cotton stopper is withdrawn from the mouth of the tube containing the solidified blood-serum and the swab then rubbed gently over the surface of the culture medium, care being taken not to break the smooth surface of the medium. The swab is then withdrawn, the cotton stopper, which must have been held so as to have escaped contamination from any outside source, replaced in the mouth of the culture-tube, the swab dropped into its tube again and confined by its own stopper. The culture-tubes are then ready for incubation. Koplik has described a rapid method of incubation and examination in which he allows only two or three hours' incubation at 37° C., at the end of which time he asserts that the growth of the diphtheria bacilli is more characteristic than at any other period of incubation.

When there is no special reason for haste, it is usually more convenient to adopt the method followed by the New York Board of Health, of twelve hours' exposure; the cultures are kept at body temperature overnight, and are ready for examination in the morning.

It is not possible to determine the presence or absence of diphtheria bacilli in the cultures upon the blood-serum from the gross appearances; but if it is found that the culture medium has been liquefied during the incubation, it can safely be said that contaminating bacteria are present in such numbers as to render the culture valueless. The diphtheria bacilli or cocci do not liquefy the medium.

Upon the center of a clean cover-glass is placed a drop of sterile water. With a sterile platinum loop a number of the colonies, which show themselves as fine, granular elevations upon the culture surface, are swept off. The loop is then immersed in the water upon the cover-glass and its contents spread evenly over the glass. The preparation after being allowed to dry in the air is fixed by passing it three times through a moderate gas flame. It is then stained by covering it with Löffler's alkaline methylene-blue solution and allowing it to stand for ten minutes, or Neisser's diphtheria stain can be used. The cover-glass is then washed, dried, and mounted in Canada balsam.

The examination is made with a $\frac{1}{12}$ oil-immersion lens. In a large proportion of the cases we see an almost pure culture of the diphtheria bacillus; next most frequently cultures of cocci, single, double, or in chains; in some cases the cocci and bacilli are about equal in number, and in a small number only a few diphtheria bacilli are seen scattered among great numbers of cocci. From time to time we see in the cultures bacilli which closely resemble the diphtheria bacilli, but with certain definite points of distinction, and pseudodiphtheria bacilli. The diphtheria bacilli seen in such cover-glass preparations vary in length from 1.5 to 6.5 mm., and in diameter from 0.3 to 0.8 mm. They occur singly or in pairs, rarely in chains of three or four. The rods are straight or slightly curved and are not usually uniformly cylindrical throughout their length, but are swelled at the ends, or pointed at the ends and swelled in the middle. The variety in size and shape, even from the same culture, is characteristic. When in pairs, the bacilli may lie with their axes in the same line or forming an acute or obtuse angle; sometimes they are crossed. The bacilli show no spores, but may contain highly refractile bodies, especially in their swelled portions. When grown upon blood-serum and stained in the manner above described, the bacilli stain in a peculiarly characteristic way. Lack of uniformity, both in the individual bacillus and in the numbers of groups, is marked. Thus, different parts of a bacillus take the stain unequally; so that the ends are dark blue, while the center shows little or no color, or *vice versâ*. Likewise bacilli lying side by side show marked difference in coloring, one being much more deeply stained than the other. This lack of uniformity in the staining of the bacilli seems to belong to a certain period of their growth; it is usually marked after the twelve-hour incubation, but may disappear entirely in older cultures.

Mention has already been made of bacilli found in cultures resembling the diphtheria bacillus and yet not possessing the specific pathogenic properties of that bacillus, and therefore termed pseudodiphtheria bacilli. This term is most unfortunate, since these bacilli bear no relation to the throat inflammation termed pseudodiphtheria. As seen in cover-glass preparations, these bacilli are shorter, plumper, and more uniform in size and staining. They are most often met with in cultures from the nose. When obtained in pure cultures, these bacilli have been shown to be devoid of virulence.

As seen under the microscope, the uniformity in size, shape, and staining is sufficiently marked from the variations in these points noted with reference to the diphtheria bacillus to enable practised observers to recognize them readily.

Whenever we find the characteristic bacilli above described present in the cover-glass preparations, we can safely set the case down as one of true diphtheria, however few the bacilli may be in number in the smear, or with whatever other bacteria combined. If the diphtheria bacilli are found at all, a second culture usually shows them greatly exceeding in numbers any other form of bacteria present, and the cases will be found to present the clinical symptoms of diphtheria.

In any case, to render the bacteriological diagnosis complete, it would be necessary to obtain the diphtheria bacilli in pure culture and test their virulence by inoculation of susceptible animals.

In routine practice this is done by inoculating half-grown guinea-pigs with from ¼ to ½ per cent. of their body weight of a forty-eight hours' culture of the bacilli grown at 37° C. in simple nutrient or glucose alkaline broth. In carrying out such experimentation many precautions are necessary to render such work accurate and trustworthy. Much time and labor are consumed in the process. For our purposes it is sufficient to know that the great majority of those who have carried on such experiments under proper conditions with bacilli derived from pseudomembranes and presenting the morphological and staining characters of diphtheria bacilli have found the bacilli fully virulent.

So long as the bacteriological diagnosis is reinforced by clinical evidence of the presence of false membrane and the symptoms of diphtheria, we can safely trust to the examination of these cover-glass preparations.

We find, however, that the examination of healthy throats has led to some remarkable results. In the throats of those who have been exposed to diphtheria, but have remained perfectly well, we may find characteristic and fully virulent diphtheria bacilli; in others we may find the pseudodiphtheria bacillus already spoken of, or a bacillus which, while presenting the cultural and morphological characters of the diphtheria bacillus, proved in inoculations to be non-virulent.

Thus, in a series of 330 healthy throats examined by the New York Board of Health, in 8 virulent characteristic diphtheria bacilli were found, in 24 non-virulent characteristic diphtheria bacilli, and in 27 non-virulent pseudodiphtheria bacilli. Since Hoffmann's observation of these bacilli, so closely resembling the Löffler bacillus, but devoid of virulence, a great deal of attention has been given to this subject. Opinion is still divided as to the relation of these non-virulent bacilli. On the one hand, they are regarded simply as degenerate or attenuated forms of the diphtheria bacillus; on the other, they are represented as a distinct species.

The identity of the pseudodiphtheria bacillus seems to be now established. In form these are smaller, shorter, and thicker than the diphtheria bacillus. When seen in stained smears the bacilli are often observed to be lying parallel to one another, in contrast to the irregularly angular disposition of the diphtheria bacillus. In their growth in broth the pseudodiphtheria bacilli develop alkali, where the Löffler bacillus forms acid. They are never virulent. These differences are, by most authorities, considered sufficient to warrant the belief that they are a separate species.

The other class of non-virulent bacilli found in the throat present all the characters of the Löffler bacillus except their virulence. Roux and Yersin believed these bacilli to be simply attenuated forms of the diphtheria bacillus. It was shown that they are particularly likely to be met with in the throats of those who have had diphtheria some time before, or have been exposed to diphtheria. It was also found that the diphtheria bacillus could be so attenuated by various methods of growth as to deprive it of its virulence. No one, however, has yet been able to restore virulence to any of the non-virulent forms met with, and the question must be considered as still open.

Diagnosis by smears is unreliable, being of value only if positive; culture examination is absolutely reliable, but has one fallacy aside from the possibility of error: it takes at least twelve hours before a diagnosis is made. Clinically we can usually recognize a probable case of diphtheria, and mistakes are rarely made; if we wait for the culture report, we have diagnosis security, but the child has less chance of recovery. If suspicious cases are treated as diphtheria, the mortality will be much lower, especially as diphtheria antitoxin is harmless and may be beneficial to patients with tonsillitis, scarlet fever, etc.

Infants and young children rarely have follicular tonsillitis, and therefore a probable diagnosis of diphtheria should be made upon slight evidence; the dangers of waiting are so great that a clinical diagnosis is of first importance and all sufficient for the purpose of treatment. F. P. Webster (Boston Med. and Surg. Jour., Nov. 21, 1907).

The authors advocate the method of Bordet and Gengou, of fixation of the complement, for a rapid, early, sure diagnosis. As antigen they employed an emulsion in salt solution of the mucus obtained from the tonsils and pharynx on a cotton tampon. Antidiphtheritic serum from the Pasteur Institute contained the amboceptor, and fresh rabbit serum the complement. A sheep hemolytic system was employed. Twenty-five cases of diphtheria resulted in fixation; 10 cases of non-diphtheritic angina, 9 of measles, and 3 of scarlatina showed hemolysis and were negative. Weille-Halle and Block-Michel (Bull. et Mém. de la Soc. Méd. Hôp. de Paris, vol. xxvii, p. 707, 1910).

The writer has simplified Schepilewsky's method. To 10 c.c. of Löffler serum composed of 3 parts of serum and 1 of broth he adds 5 drops of fuchsin solution. Once sterilized and solidified, this medium receives the supposed diphtheritic material and is placed in a thermostat for twenty-four hours. If diphtheritic bacilli are present, a vivid-red color appears, produced by the acids generated by the micro-organisms, while if they are not the color is light rose. Löffler's bacilli give this reaction in twelve hours. In thirty-six hours the red becomes less vivid and in forty-eight has disappeared. As shown by a large number of cases, this reaction is a conclusive diagnostic sign. E. Cionini (Gaz. Tuber. Med., May, 1910).

New stain for the demonstration of *B. diphtheriæ*. The mixture consists of: Glacial acetic acid, 5 c.c.; distilled water, 95 c.c.; alcohol, 95 per cent., 100 c.c.; old saturated aqueous solution of methylene blue, 4 c.c.; Ziehl's carbol-fuchsin, 4 c.c. This mixture is spread over the preparation in a thin layer and drawn through the flame. The alcohol ignites and burns in eight or ten seconds. After the stain is allowed to act five to six seconds longer, it is washed off with water, the specimen blotted dry, and examined. The polar granules are stained deep blue, the bodies of the bacilli bright red. Even when diphtheria bacilli are few in number in a mixed culture, they are readily seen. The whole procedure requires only twenty to twenty-five seconds. The stain may be kept indefinitely. Marie Raskin (Amer. Jour. Med. Sci., from Deut. med. Woch., Bd. xxxvii, S. 2384, 1911).

Very accurate results in the recognition of diphtheria bacilli may be obtained by the use of a medium composed of sheep's blood serum, 3 parts; bouillon, 1 part; glucose, 0.5 per cent.; potassium sulphocyanide, 1 part; and 2 per cent. of a 5 per cent. solution of neutral red. The bacillus of diphtheria grows in rose-colored colonies, which are readily distinguished from the colonies of those few other microbes (chiefly cocci), the growth of which is not retarded by the medium. Rankin (Jour. of Hygiene, vol. xi, 1911).

New culture medium for isolating the diphtheria bacillus. Ten Gm. of meat extract, 5 Gm. of sodium chloride, 20 Gm. of peptone [Witte] and 6 Gm. of calcium acetate are added to 1000 c.c. of water. The mixture is placed over the water-bath for one-half hour and filtered. The filtrate is slightly acid and 1 per cent. of grape-sugar is added to it. One part of this mixture is added to 3 parts of fresh sterile blood-serum and to 100 c.c. of this blood-serum mixture 2 c.c. of a 1 per cent. solution of potassium tellurite is added. The mixture is then shaken and distributed in Petri dishes. The original culture of the suspected material is made on Löffler's blood-serum. The culture is incubated for three hours at 35 C. and then a culture is made from it on the tellurium plate. This plate is incubated for twenty hours at 35 C. and the original Löffler plate is allowed to continue development and growth for eight hours so as not to interfere with examination of such bacilli as have developed in this plate. If diphtheria colonies are visible on the Löffler plate, further examination of the tellurium plate is unnecessary. If, however, the former fails to show any diphtheria cultures, the latter must be examined. The diphtheria colonies will be colored black, the result of a reduction of the tellurium dioxide. Even the diphtheria bacillus contains these dark spots. The authors have had splendid results clinically from the use of this method of examination. Conradi and Troch (Jour. Amer. Med. Assoc., from Münch. med. Woch., July 23, 1912).

Toluidin blue gives a better differentiation than any yet devised, and the technique is simple. The writer uses toluidin blue, 0.02 Gm.; glacial acetic acid, 1 c.c.; absolute alcohol, 2 c.c.; and distilled water to make 100 c.c. A smear is taken fresh from the throat, and, when fixed on a cover-glass, is stained by placing a thin drop of the stain directly upon it and inverting it to make a hanging-drop preparation. This is then examined by artificial light, the blue of the fluid tending to neutralize the yellow rays. The diphtheria bacilli stain a light blue with red granules, and are refractive. It is possible to differentiate them from pseudodiphtheria bacilli at once. Ponder (Lancet, July 6, 1912).

ETIOLOGY.—As early as 1879 Klebs is said to have observed the presence of a peculiar bacillus in cases of diphtheria. In 1883 his observations of the presence of this bacillus in the pseudomembranes from the throats of those dying of epidemic diphtheria were reported and brought to general attention. In 1884 Löffler published the results of his observations. He had found the bacillus present in the great majority of cases diagnosticated as diphtheria, had been able to obtain the bacillus in pure culture, had inoculated it upon the abraded mucous membranes of susceptible animals and thereby produced pseudomembranous inflammation, often followed by death; he had injected bouillon cultures of the bacillus subcutaneously and had found characteristic lesions after the death of the animals so treated. In 1888 d'Espine found the bacilli present in 14 cases of typical diphtheria, and proved them to be absent in 24 cases of mild sore throat not presenting the clinical characters of diphtheria. In the same year Roux and Yersin reported that they had found bacilli presenting the characters described by Löffler in all cases of typical diphtheria. They showed that when inoculated upon the healthy mucous membrane of the trachea of rabbits no effect was produced; but, if the membrane were previously abraded the symptoms of pseudomembranous laryngitis in man followed: congestion of the mucous membrane, the formation of pseudomembrane, swelling of the glands and cellular tissues of the neck, dyspnea, stridor, and asphyxia. From that time on numerous observations were made in France, Germany, and America, until, in 1891, Welch declared that all the conditions necessary to the demonstration of the specific relation of the Klebs-Löffler bacillus to diphtheria had been met: (1) its constant presence in cases of true diphtheria; (2) its isolation in pure culture, and (3) the production of all the symptoms of the disease by the inoculation of pure cultures in susceptible animals. Since that time evidence has been accumulated from many sources, till there can no longer be any doubt that the essential cause of diphtheria is the growth and development of this bacillus within the body. The development of the disease must, therefore, be dependent in every case upon the presence and action of the diphtheria bacillus.

The disease is common in all parts of the land. In the cities it is usually endemic, the frequence and virulence of the disease varying from year to year; in rural communities it usually occurs as distinct epidemics, each new outbreak being dependent upon the introduction of the disease from without. It may also occur sporadically. It does not, however, in any case arise *de novo*. Each new case is developed by infection, however remote, from some previous one. The infection may be either direct or indirect. Direct infection is undoubtedly most common.

The bacilli are usually present in great numbers in the discharges from the throat or nose of the patients, in the saliva, and in the membranes which may, from time to time, be coughed up. They are not, so far as evidence is had, present in the breath of the patients, but may abound in the air of the room or rooms inhabited by them. The bacilli have even been reported as present in the urine of patients.

Direct contact with the discharges from the nose or throat of those suffering from diphtheria is most dangerous. Many a physician has fallen victim to diphtheritic infection received by allowing a child to cough in his face during the process of examination. Kissing the patients may likewise be the means of infection in many cases.

While severe cases are usually due to the action of virulent bacilli and may, therefore, be especially potent in transmitting the disease, it is not to be forgotten that apparently mild cases may harbor bacilli just as virulent and just as much to be avoided. As already remarked, the most virulent bacillus Park has met with was derived from a mild case of diphtheria. The cases of virulent pharyngeal diphtheria are most dangerous on account of the quantity of the discharge. Purely laryngeal cases have little or no discharge, and are consequently less likely to spread the infection.

The bacteria may linger in the throat for weeks after the disappearance of all clinical symptoms and the patients continue throughout the period to be sources of infection.

Indirect infection may occur by means of the clothing of the patients, the bedding, carpets, wallpaper, draperies, eating or drinking utensils, tongue-depressors, swabs, instruments of any kind used upon or about the patient, anything that has come in contact with the infectious discharges. Children's toys or books are especially likely to be contaminated and become means of carrying the germs to others.

The urine has been found to contain diphtheria bacilli long after the patient had recovered, several months in some instances. They have also been found in feces.

The writer, with Haas, has published an article on anal diphtheria, and the presence of bacteria in the feces. This makes it imperative to disinfect these excreta as well as the urine. Delbanco (Deut. med. Woch., Nov. 12, 1912).

Virulent diphtheria bacilli reach the urine in about one-third of all cases and are often in position to propagate the infection. The danger of direct contact infection is slight because of the great dilution, there being relatively few bacteria present in a given bulk of urine. Yet under favorable conditions the urine might contaminate the milk vessels and so infect a milk supply. In theory the urine might infect the patient's skin, causing, for example, diphtheritic vulvitis. Conradi and Bierast (Deut. med. Woch., Aug. 22, 1912).

Diphtheria bacilli found in the urine in all of 19 children examined when they had supposedly entirely recovered from diphtheria. The interval at date of writing was from four to eight weeks up to fourteen weeks, and in 6 of the 8 cases in which animals were inoculated with the bacilli they proved virulent. Strict hygiene would require the isolation of the children until the urine was free of bacteria. Beyer (Münch. med. Woch., Feb. 4, 1913).

Apart from the question of the transmission of the disease from case to case, many other factors may influence the development and spread of diphtheria.

Sex apparently has no influence, but age materially influences the susceptibility. Nursing children are usually immune and contract the disease only by continued close contact with those suffering from it. The greatest susceptibility lies between the ages of 2 and 5 years; from 5 to 10 many cases are seen; after 10 the susceptibility diminishes very rapidly, and in adults it is but slight. The following table of 14,688 deaths occurring in New York in ten years, tabulated by Billington, illustrates these points:—

Under 1 year	1,214
From 1 to 5 years	9,622
From 5 to 10 years	3,212
From 10 to 15 years	311
Over 15 years	329
Total	14,688

Case of diphtheria occurring in a woman aged 79 years. The diagnosis was confirmed by bacteriological examination, and treatment with diphtheria **antitoxin** was followed by a gradual recovery. The patient had suffered for years from gouty stiffness and neuritis. Two hours after the antitoxin injection all stiffness and pain had disappeared. The author has seen a similar effect produced by an attack of pneumonia in a gouty patient. Birt (Lancet, Nov. 18, 1905).

The season of the year exerts some influence. Thus, in England and Wales the average number of deaths for each quarter of the year, from 1870 to 1893 inclusive, was as follows: First quarter, 1000. Second quarter, 819. Third quarter, 847. Fourth quarter, 1192. (Thorne.)

Diphtheria is, therefore, more common during the cold months of fall and winter than during the spring and summer. The same fact is borne out by Bosworth's analysis of 18,688 deaths from diphtheria occurring in New York during thirteen years. Of these, 10,769 occurred from October to March, and 7919 from April to September, inclusive.

The massing of children in schools, asylums, and hospitals produces conditions favorable to the development and spread of diphtheria, doubtless by increasing the chances of infection. The schools have often been pointed out as the sources of epidemics of diphtheria, which could only be controlled by closing the institutions concerned.

The following section from the Bulletin of the New York Board of Health is of interest in this connection:—

"It has been the practice of the Department to plot upon a city map the location and date of every case of diphtheria in which the diagnosis had been settled by bacteriological examination. After several months the map presented a very striking appearance. Wherever the densely settled tenements were located, there the marks were very numerous, while in the districts occupied by private residences very few cases were indicated as having occurred. It was also apparent that the cases were far less abundant, as a rule, where the tenements were in small groups than in the regions of the city where they covered larger areas. At the end of six months there were square miles in which nearly every block occupied by tenement houses contained marks indicating the occurrence of one or more cases of diphtheria, and in some blocks many (15 to 25) had occurred.

"As the plotting went on, from time to time the map showed the infection of a new area of the city, and often the subsequent appearance of an epidemic. It was interesting to note two varieties of these local epidemics: in one the subsequent cases evidently were from neighborhood infection, while in the second variety the infection was as evidently derived from schools, since a whole school district would suddenly become the seat of scattered cases. At times, in a certain area of the city from which several schools drew their scholars, all the cases of diphtheria would occur (as investigation showed) in families whose children attended one school, the children of the other schools being for a time exempt."

A number of epidemics have been

traced to infected milk, the infection arising from the presence of diphtheria among those engaged in handling the milk.

Certain English observers have also claimed to have discovered a specific disease among milch cows, characterized by an eruption of vesicles and pustules upon the udders and teats, accompanied by the presence of the diphtheria bacillus in the local lesions, and capable of being reproduced by infections of the bacilli.

> Epidemic of diphtheria which could be traced to milk. In the family of a farmer, who sold milk to a dealer, was found the source of infection. A member of this family was seized with the disease; the cooler in which the milk was mixed was washed in the house by the person who had charge of the sick member. The farmer himself came down with the disease, and the dealer's son, who drank from the milk, was one of the earliest victims. Prompt action on the part of the local authorities in excluding from sale the milk of the farmer brought the outbreak to an immediate close. Harrington (Boston Med. and Surg. Jour., June 27, 1907).

Other outbreaks of diphtheria have been attributed to bad drainage, defective sewers, or the presence of an abundance of decomposing organic matter. It is also held that certain domestic animals—pigeons, cats, etc.—are susceptible to diphtheria and may be the means of transmitting it to man.

> Two cases of wounds which have become infected with the diphtheria bacillus. One of the cases was that of a finger, infected in the lumber woods, which had been opened and dressed, but refused to heal. When seen three months later, there was tremendous induration in the axilla, with three sinuses. Actinomycosis was suspected, but pure cultures of the diphtheria bacillus were found on examination. Antitoxin treatment resulted in cure. Tuohy (N. H. Lancet, May 1, 1909).

However much or little insanitary surroundings may contribute to the development of diphtheria, the active and essential cause must be the diphtheria bacillus, and our hope of limiting the ravages of this disease must be based upon control of the individual cases, each of which is a focus for the farther spread of the infection.

The tenacity to life of the bacillus outside the body is remarkable. Hofmann found that it would live for 155 days on blood-serum; Löffler and Park for 7 months, and on gelatin Klein found it living after 18 months. On bits of dried membrane Klein found living bacilli after 14 weeks, Park after 17, and Roux and Yersin after 20 weeks. Abel says that, dried on silk threads, they may live 122 days, and upon a child's plaything kept in a dark place he found the bacilli alive after 5 months.

The period of incubation of diphtheria varies from two days to a week. It is doubtless affected by the number and virulence of the organisms present and by the resisting power of the patient. In most cases it is impossible to determine the time of exposure, much less that of infection. Second attacks of diphtheria are rare, but do occur. In one case observed at the New York Foundling Hospital, a boy of 4 had croup in March. The diphtheria bacilli were demonstrated in cultures from the throat. Antitoxin was given and he recovered. Twenty-five days later, having been apparently well in the mean time, he developed tonsillar diphtheria, which extended to the larynx, pneumonia developed, and death followed, thirty-four days from the conclusion of the first attack. According to Zucker, second or third attacks comprise 9 to 13 per cent. of all cases of diphtheria.

Transmission by Carriers.—In some cases persons who are themselves perfectly healthy, but who have been in contact with diphtheria cases, are found to harbor the bacilli in the nose or throat and may be the source of infection to others. On several occasions the development of a series of cases of diphtheria in a single nursery of the New York Foundling Hospital has led to the examination by cultures of the throats of all children in that nursery, with the result of usually finding two or three who, while apparently healthy, had typical germs in their throats.

Among well school-children approximately 10 per cent. harbor in their throats bacilli which correspond morphologically with the organisms of diphtheria. One-half of these organisms were without effect on guinea-pigs; about 30 per cent. behaved like attenuated forms, and 14 per cent. killed the animals with a fair degree of promptness. Of 25 strains of diphtheria bacilli obtained during the last days of convalescence, 23 were highly virulent and only 2 without virulence. One case gave a virulent organism on the eighteenth day and a non-virulent one on the thirty-fifth day. Pennington (Jour. of Infect. Dis., Jan., 1907).

Three cases of diphtheria having developed in a military school, the patients were isolated at once and no epidemic followed. To determine whether there were any healthy bacilli carriers in the school, bacteriolgical tests were made of secretions from the throat of every inmate of the institution—185 individuals. In 40 cases the findings were suspicious as bacilli resembling the diphtheria bacilli were found, but never the genuine diphtheria bacillus except in the three convalescing patients. In these convalescents virulent diphtheria bacilli were found up to the fourth, eighth and ninth week after recovery, and these strains were very virulent for guinea-pigs. The experiences related testify against the ubiquity of the diphtheria bacillus, while they confirm the importance of early and complete isolation of the patient until the diphtheria bacilli have disappeared from the secretions of nose and throat. Hasenknopf and Rothe (Jahrbuch für Kinderheilkunde, Oct., 1907).

Case of a woman, 22 years of age, who recovered from an attack of diphtheria, but more than a year later continued to complain of her throat and to have occasional attacks of fever. She was also known to have communicated diphtheria to 2 other persons more than a year after her recovery. Smears taken from her fauces and tonsils showed the abundant presence of Löffler's bacilli which presented all their characteristics and were virulent for animals. Gabriel (Berl. klin. Woch., June 8, 1908).

It is the latent and "carrier" cases that are mostly responsible for the prevalence of diphtheria in cities where the usual precautions are taken in regard to clinical cases that are reported or "notified" to the health authorities. Not until these hitherto unrecognized cases are discovered and removed as sources of contagion will much headway be made in checking the spread or preventing the occurrence of diphtheria. Meyer Solis-Cohen (Jour. Amer. Med. Assoc., Jan. 9, 1909).

Diphtheria epidemic in the Connecticut Hospital for Insane, lasting from April, 1907, until May, 1908. There occurred 92 cases, 57 of which were in employés and 35 in insane patients. During this period the throats of 4081 healthy individuals were examined, with the result that 95 (2.08 per cent.) revealed the presence of the Klebs-Löffler bacillus, so that the total number of people under quarantine was 187. The early diagnosis, made possible by careful culturing, permitting of early treatment with antitoxin, undoubtedly diminished the severity of the individual case, and the severity and duration of the epidemic. Of healthy individuals during epidemic 2.08 per cent. were found to be bacillus carriers. When no epidemic existed non-virulent Klebs-Löffler bacilli were found in 1.1+ per cent. of healthy individuals. No virulent Klebs-Löffler bacilli were found in 506 throat cultures three months after epidemic. Fisher (Jour. Amer. Med. Assoc., Feb. 6, 1909).

A diphtheria epidemic in the Brighton district of Boston showed that at least 1 per cent. of all healthy school-children are carriers of morphologically typical diphtheria bacilli. Such bacilli are communicable from one person to another and the condition is usually a transient one, but are ordinarily of little or no virulence. While it is possible that by passing through a susceptible individual their virulence might be raised to cause the disease, this is not a frequent occurence. The disease diphtheria is kept alive in a community rather by virulent organisms in immune persons than by these non-virulent bacilli. Slack, Arms, Hade and Blanchard (Jour. Amer. Med. Assoc., March, 1910).

Analysis of the findings by throat cultures as regards the diphtheria bacillus during the year ending Oct. 31, 1910, at the bacteriological laboratory of the Indiana State Board of Health. The total number of cultures was 2288, 624 of which, or 27.2 per cent., were positive. The influence of school attendance on the incidence of diphtheria was quite marked, as shown by the following: Contrary to the figures given by investigators in England and Wales, where the greatest incidence of the disease was found in the first five years of life, only 17 per cent. of positive first cultures were found in children under school age, while 58 per cent. were from patients between 6 and 14, and 12 per cent. from patients between 15 and 20. The average number of first cultures per month during the vacation period was 16, as contrasted with a monthly average of 77 during the school term. J. P. Simonds (Jour. Amer. Med. Assoc., Jan. 7, 1911).

Nineteen cases in which the child was well, the throat findings negative, but cultures taken from the mother's throat the day the child left the hospital were positive. The bacilli from the throats of the diphtheria carriers are as virulent as those in the throats of the sick. Diphtheria bacilli may linger in the throat for months after the patient is well. These bacilli carriers and convalescents are particularly dangerous for spreading the bacilli. Patients should remain in the hospital until their throats are free from diphtheria bacilli, but they may, on returning home, become infected again from bacilli carriers in the family. Sommerfeld (Archiv für Kinderheilkunde, Bd. lvii, Nu. 1-3, 1912).

The isolation of these children would at once break the succession of cases of diphtheria previously observed. It may also happen that physicians or nurses transmit the germs either by their hands or clothing from one case to another. The frequent occurrence of diphtheria in the families of physicians is sufficient evidence of the need of care.

During the twelve years 7037 cases of diphtheria were treated at the Blegdam Hospital at Copenhagen. There were 82 fresh cases of diphtheria among members of their families after the patients had returned home, or a proportion of 1.16 per cent. Of the 82 patients who were the apparent cause of infection, 81 had been examined bacteriologically, and only 8 showed the presence of diphtheria bacilli in the throat. Of the 7037 diphtheria patients during the twelve years about 700 were carriers of the Löffler bacillus when they returned home, and yet these 700 patients only supplied 8 "return cases," or 1.14 per cent.—that is, almost the same proportion as given above, 1.16 per cent. It appears, therefore, that the bacillus carriers are not more dangerous to their families than those ascertained by bacteriological examination to be exempt. In other words, according to these statistics, the bacteriological examination of the throat, upon which so much stress has been laid recently, would appear to have by no means the same value that has been attributed to it as a means of determining the infectibility of a patient after an attack of diphtheria. The "return cases" were not specially severe, and there was not a single fatal case among them. Sörensen (Hospitalstidende; The Hospital, Sept. 30, 1911).

PATHOLOGY.—The bacteriological investigations of recent years have materially affected our views of the pathology of diphtheria. We have learned that the local lesions of the mucous membranes really constitute a very subsidiary part of the process. In them the diphtheria bacilli grow and multiply, developing in their growth certain organic substances, termed toxins, which are readily absorbed into the circulation and by their action produce constitutional symptoms and remote affects more characteristic of the disease than the local lesions themselves. The diphtheria bacilli have been found not only upon the mucous membranes, but in the lungs, liver, spleen, lymph-nodes, kidneys, and even upon the valves of the heart. They are not, however, present in great numbers in any of these organs; in fact, they are, except possibly in the case of the lungs, so few in number as to be demonstrable only by means of cultures. Their presence in the viscera does not excite characteristic lesions of these parts, and seems to be an accidental accompaniment rather than an essential part of the disease.

The diphtheria bacillus present in the blood and cerebrospinal fluid. In the blood it is said to occur in less than 5 per cent. of cases. The bacillus likewise enters the cerebrospinal fluid in at least one-half of all cases. In a study of the lungs at the Hamburg-Eppendorf Hospital, in 67 cadavers (of which number 43 had died during the period of disease and the rest after the disease proper had run its course) diphtheria bacilli were found in the lungs in 56 subjects (85 per cent.). In all but 6 cases of the positive finds other bacteria were present, chiefly erysipelatous streptococci. In the negative cases the microbic finds were insignificant. The association of the Klebs-Löffler and Fehleisen bacteria in so many cases (27 in all) was at least suggestive. Reye (Münch. med. Woch., Oct. 29, 1912).

The action of the toxins is characteristic and important. These substances have been isolated and studied especially by Brieger and Fraenkel, Roux and Yersin. They have been found to be allied to the albumins, and have been designated as toxalbumins. In experimental inoculations in susceptible animals, as shown by Welch and Flexner and others, they have been found to produce all the characteristic features of diphtheria except the membrane, especially the characteristic post-diphtheritic paralysis. The most striking of their remote effects are produced in the lymph-nodes and liver. In the lymph-nodes they produce a distinct hyperplasia; in the liver necrosis or death of small areas of liver-cells, focal necroses, similar to those seen in the liver in typhoid fever and other infectious diseases.

We must, therefore, believe that the presence of these soluble poisons in the circulation constitutes a very important feature of diphtheria. These toxins, as already noted, are elaborated in the local lesions of the mucous membranes, and not by the bacteria that may be present in the various viscera. The quantity and quality of the toxins generated seem, as a rule, to be proportionate to the severity of the local process.

The presence of toxins circulating in the blood, and the possibility of their being the cause of diphtheritic paralysis were studied by the writer. He injected diphtheria toxins into rabbits, and found that they always caused a gelatinous infiltration at the site of injection. He then injected them with the blood of infants sick with diphtheria in various stages, and found that in the early stages this gelatinous exudate was produced, but that later in the course of the disease it was absent. Toxins were found for several days after the disappearance of the exudate in the throat; but later than this there was no evidence of their presence in the circulation. Gino Menabuoni (Riv. di Clin. Ped., Jan., 1910).

Catarrhal Diphtheria.—As we have already seen, the local effects of a diphtheritic inflammation vary greatly. In catarrhal diphtheria we see simply redness and some swelling of the mucous membrane of nose, throat, tonsils, or larynx, usually with an increased secretion of the mucous glands. None of these would show macroscopically in the rare cases when death follows such a process. Oertel has, however, found in these cases degeneration of the epithelial cells of the mucous membranes similar to those seen in pronounced cases of diphtheria.

The Diphtheritic Membrane.—The membrane is most frequently seen upon the tonsils, soft palate, uvula, pharynx, nares, larynx, trachea, or bronchi. In severe cases it may appear upon the lips, especially at the angles of the mouth, the buccal mucous membrane, and the tongue. Very rarely it appears in the esophagus, stomach, or intestines. In fact, the freedom of the esophagus, when the diphtheritic membrane may be seen completely covering the pharynx and tonsils and extending throughout the whole respiratory tract even to the terminal bronchi, is most remarkable. Even in the severest cases the membrane usually stops abruptly at the beginning of the esophagus.

It is also possible to observe a true diphtheritic membrane upon abraded cutaneous surfaces; upon wounds, as in tracheotomy, or upon the conjunctiva or the genital mucous membrane. The color of the membrane may be white, gray, greenish white, yellow, or more or less black when there has been hemorrhage from the affected surfaces. It may be thick and elastic, so as to be stripped off in sheets, or thin and diffluent. The thicker membrane is observed upon the surfaces covered with columnar epithelium, with a definite basement membrane, such as the nose, larynx, trachea, and bronchi. Here, too, it is but loosely attached; so that it is often thrown off in casts during life, or after death may easily be stripped off from the underlying surfaces. Upon the tonsils, pharynx, uvula, and fauces, where the epithelium is of the squamous variety and without a basement membrane, the diphtheritic membrane is much more closely attached. Often in these situations we see, after death, no distinct membrane, but a diffluent exudate, which may be easily washed off, leaving a distinctly ulcerated surface beneath.

Microscopically the membrane or exudate is found to consist chiefly of fibrin, mingled with epithelial cells from the mucous membrane; pus-cells, red blood-cells, granular material, and bacteria. The superficial parts of the membrane are granular in character, while beneath we find a more or less distinct network of fibrin, inclosing within its meshes the cells, granular material, and bacteria. The bacteria are the diphtheria bacilli together with streptococci or staphylococci, and rarely pneumococci. The inflammatory process may be superficial or may extend irregularly into the mucous membrane, in some cases involving the submucous tissue and even the muscular coat. The bacteria may likewise penetrate deeply into the tissues, but are usually most abundant in the superficial parts of the membrane. The epithelial cells of the mucous membrane undergo degeneration, their protoplasm becoming granular, their nuclei fragmented, and the cells ultimately breaking up into granular material. The pathological process is, therefore, a coagulation necrosis involving the mucous membrane more or less deeply.

The pseudomembrane is cast off in masses or is gradually disintegrated, with more or less destruction of the mucous membrane. The process of separation is usually attended by a more abundant cellular exudation beneath the pseudomembrane. Except in the gangrenous cases apart from the tonsil, in which there may be extensive destruction of the tissues, the integrity of the mucous membrane is completely restored, leaving no traces of the preceding disease. Gangrene is not properly a part of the diphtheritic process, but is caused either by especially unfavorable conditions affecting the vitality of the patient or by the invasion of unusually virulent bacteria other than the diphtheria bacilli, probably the streptococci.

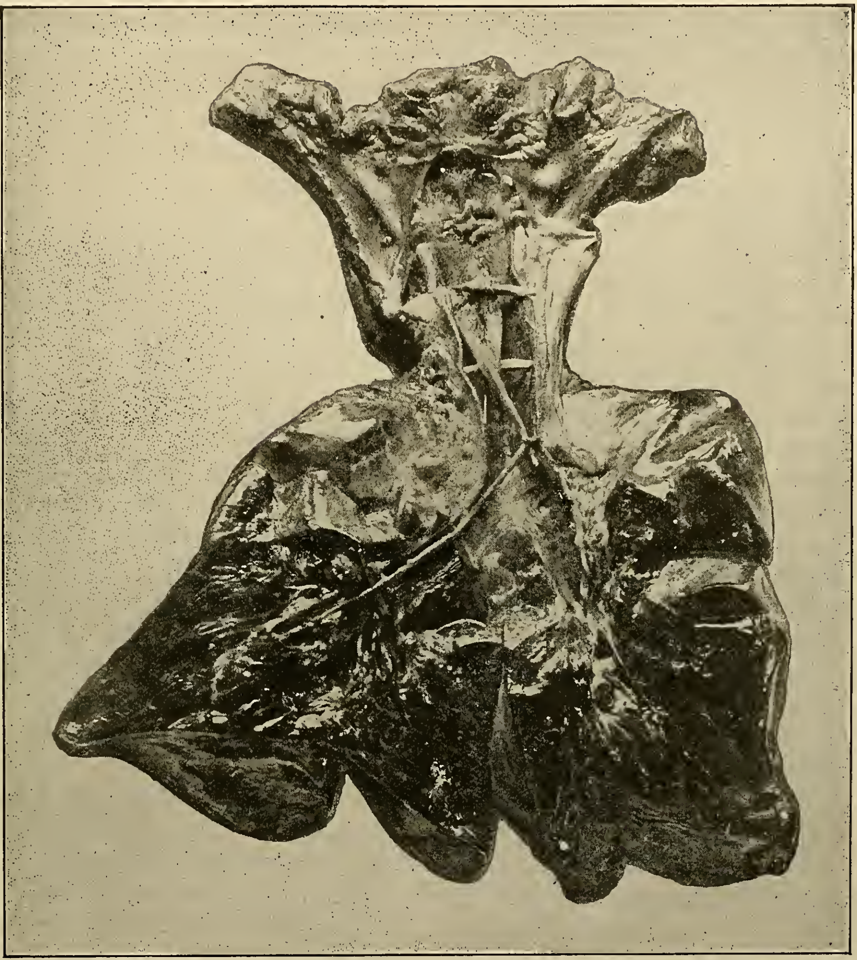
The seat and distribution of the membrane vary greatly in different cases. The point of importance with reference both to symptoms and prognosis is the involvement of the larynx. Of 1000 cases analyzed by Lennox Browne, the larynx was involved in 159, in only 4 of which number was the affection limited to the larynx. In a similar analysis of 109 cases by Holt, the larynx suffered in 46, in 10 of which the disease involved either the larynx or the larynx with the trachea or bronchi. Holt gives no purely nasal cases in his series; 2 are given by Browne. In the great majority of cases the membrane is found upon the tonsils or the adjacent parts, the pharynx, uvula, and pillars of the fauces. Six hundred and seventy-two of Browne's 1000 cases showed such distribution.

Since extension of the membrane usually increases the severity of the case and the probability of death, the clinical records of Browne show the comparative frequency of the various forms better than tables which are largely formed from autopsy records. Laryngeal cases are also much more frequently met with in children's hospitals or asylums than in dispensary or private practice.

In cases involving the nasal cavities the process is often catarrhal, and there may be no macroscopic lesion after death. In many such cases, however, there may be membrane in the rhinopharynx, the adenoid tissue of the vault of the pharynx being a favorite seat of the disease. When membrane is developed in the nose, it is usually thick and but loosely attached; so that it may readily be thrown off as casts of the nares.

Upon the tonsils the membrane may be found only in the crypts, resembling a follicular tonsillitis, or it may be in scattered patches, or may completely cover the surface. It is closely adherent. The tonsils are swelled and may even meet in the median line. In most cases the membrane spreads to the surrounding parts: the pharyngeal walls, the fauces, or uvula. The epiglottis is also frequently involved in these cases, even when the larynx is not affected. The membrane often extends into the rhinopharynx and thence may pass to the Eustachian tubes and the middle ear. Upon the uvula or fauces the membrane is usually thicker and more loosely attached than that upon the tonsils.

The uvula is swelled and edematous. The epiglottis, if involved, is swelled and thickened, and one or both surfaces may be covered with membrane. After death the membrane upon these parts does not show as clearly as during life, and we are apt to find a more or less marked ulceration of the parts. The epiglottis frequently shows considerable destruction of the mucous membrane. Microscopically the pathological process may extend deeply into the submucous or even the muscular coats of these parts, but the ulceration rarely extends beyond the superficial epithelium. In cases where the membrane appears upon the pharyngeal walls it will be found to stop short at the level of the cricoid cartilage, the esophagus being perfectly normal.



Diphtheria of tonsils, larynx, trachea, and bronchi. At upper end the tonsils and base of tongue are seen. The tonsils showed superficial ulceration, covered by thin membrane. Epiglottis is thickened. Right ventricle of larynx filled by exudate and obliterated. From left vocal cord hang some shreds of membrane. Immediately below vocal cords membrane completely covers larynx and trachea. Lifted on the skewers it contracts to a rope-like strand, which is seen extending to finest bronchi on right side. Both lower lobes of lungs consolidated by pneumonia.

The appearances in the larynx are quite different from those met with in the throat. The laryngeal process may be simply catarrhal, even when there is abundant membrane in the throat and there have been marked laryngeal symptoms; so that the larynx after death may appear normal, or there may be a slight congestion of the mucous membrane and the vocal cords after death. In other cases we see a finely granular deposit upon the cords and mucous membrane, and the ventricles of the larynx may be filled by a yellowish-white exudate, but there is no distinct membrane. Again, we may see a distinct membrane masking the cords, obliterating the ventricles, and covering the mucous membrane below.

When there is either exudate or pseudomembrane present in the larynx, it is rarely limited to that part, but will be found to extend into the trachea and bronchi, and even the lungs. In the trachea we may see scattered areas of membrane, or the membrane may line the whole extent of the respiratory tract. There is usually a much more distinct membrane in the trachea than in the larynx itself. Upon these surfaces the membrane is but loosely attached; so that it may be coughed up in complete casts of the bronchial tree, or after death may be readily lifted from the underlying tissues (see illustration).

In a series of autopsies upon 87 cases of laryngeal diphtheria made by one of us (Northrup) the distribution of the membrane was given as follows: In 9 cases the membrane extended from the tip of the nose to the finest bronchi; in 6 from the nose to the bifurcation of the trachea; in 17 from the pharynx to the finest bronchi; in 17 from the larynx to the finest bronchi; in 17 from the pharynx to the main bronchi; in 17 in the larynx and trachea; in 3 in the pharynx and larynx, and in 1 in the larynx only. This work was done in the preantitoxin days, and it must be said that in the autopsies made since the introduction of antitoxin such extensive distribution of membrane is but rarely met with.

Pseudomembrane may be found in the stomach or intestines, but is rarely, if ever, produced in these situations by the action of the diphtheria bacillus; streptococci are usually found. Occurring upon the conjunctiva, the lips, buccal mucous membrane, or the tongue, the diphtheritic membrane does not present any unusual features.

Diphtheria toxin was found by Rosenau and Anderson to produce, in about 66 per cent. of guinea-pigs, round peptic ulcers in the stomach, but that the intestines are not so affected. M. V. Tyrode (Boston Med. and Surg. Jour., Nov. 19, 1908).

Upon abraded skin surfaces or upon wounds—especially the tracheotomy wound in laryngeal cases—the membrane may be pronounced, and is usually reproduced with remarkable rapidity after removal.

Apart from the lesions produced by the diphtheria bacilli at or by extension from the site of inoculation, they appear to produce no other direct effects, although they may be found present in the viscera. Their toxins, on the other hand, produce definite and characteristic visceral lesions. The experimental work of Welch and Flexner, Abbott, and others has served to make known these remote effects of the toxins. In the great majority of cases of human diphtheria, other bacteria, especially streptococci, are present and active besides the specific bacilli; they are mixed infections, and the problem of determining the action of any one organism is greatly complicated. In forty-two autopsies in cases of diphtheria in which the Löffler bacillus had been demonstrated during life, Reiche is reported to have found streptococci and staphylococci in the kidney or spleen, and streptococci alone in 45.2 per cent. Streptococci were found in the kidney in one case which died on the second day, and positive results were also obtained on the third and fourth days. The results obtained by experimental inoculation of the toxins in susceptible animals are, therefore, much simpler and more easily interpreted than examinations of the viscera of fatal cases of human diphtheria. The lesions produced by the toxins are found in the lymph-nodes, liver, kidneys, spleen, heart muscle, the peripheral nerves, and lungs.

Welch and Flexner have shown that these visceral lesions are produced either by injections of pure cultures of the diphtheria bacillus or by inoculation of their toxins.

The lymph-nodes—cervical, bronchial, mesenteric, axillary, and inguinal—are found to be swelled. There are hemorrhages either beneath the capsule or into the substance of the glands. The cells show more or less advanced degenerative changes both in their nuclei and in the cell-protoplasm. The nuclei are fragmented; the cell-bodies are converted into a finely granular, reticulated material, apparently fibrinous. Similar changes are observed throughout the lymph-structures of the body, Peyer's patches, solitary and agminate follicles of the intestines, etc. The changes in the lymph-nodes rarely lead to suppuration.

The spleen is swelled and usually softened. There may be hemorrhages beneath the capsule or into the substance of the organ. The follicles are enlarged, and the cells show degenerative changes similar to those seen in the lymph-nodes. The liver shows hemorrhages either upon its surface or within its substance. There may be an advanced fatty degeneration of the liver. There are also found minute areas in which there has been produced a necrosis of the liver-cells, the nuclei being fragmented or having completely disappeared, while the bodies of the cells show advanced degenerative changes. Some of these areas are infiltrated by leucocytes. Similar focal necroses in the liver have been observed by other poisons than the toxins of diphtheria.

The changes in the kidney include a degeneration of the epithelium of the tubes and glomeruli and hyaline alteration of the glomerular capillaries and smaller arteries. The severe affections of the kidney, acute exudative or diffuse nephritis, met with as complications of the later stages of the disease, are attributable rather to the accompanying streptococcus infection than to the diphtheria itself.

The heart shows a fatty degeneration of its muscles, sometimes so advanced as to produce changes in every fiber. The nuclei of the muscles may also be fragmented.

> One of the most striking and constant histological changes in the organs of patients dying of acute diphtheritic toxemia is an extensive fatty degeneration of the muscle of the heart and the diaphragm. These changes were found both in human cases and in animals killed by doses of diphtheria toxin. These changes are rarely detected macroscopically, but microscopically are visible as fine medium-sized or coarse droplets, filling the cells. Dudgeon (Brain, part cxiv, p. 227, 1906).
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> The two chief cardiac lesions in diphtheria are the parenchymatous and the interstitial. Fatty degeneration is extremely frequent, varying widely in degree and always accompanying the severer lesions. It may occur at any time in the disease. A much severer degeneration, both focal and general, which affects all parts of the muscle-

fiber, the contractile elements, the protoplasm and the nucleus, and which leads to the formation of granular detritus and large irregular hyaline masses, also occurs. This is only found late in the course of the disease, rarely earlier than the seventh day. The interstitial changes are of two types. In one there are focal collections of lymphoid and plasma cells. In the other there is invasion of the degenerated and necrotic muscle cells with endothelial cells and polymorphonuclear leucocytes. These are all essentially late changes. Only fatty degeneration is seen before the sixth or seventh day. The early circulatory disturbance is extraordinarily severe, but, thanks to antitoxin, is rarely seen at present. Romberg's and Passler's experiments show that this is due to failure of the vasomotor center, though undoubtedly the heart itself is affected. The late circulatory disturbances may appear at any time from the second to the fifth week. The first symptoms are usually to be found in the pulse, which drops with the temperature, often to below normal, remaining there or rising and falling again. In a certain percentage of cases it may be persistently high, but either of these means almost certainly myocarditis. At other times the first symptom is irregularity in the force or rhythm and the former is constantly present and may last for months. The worst prognosis is given in cases with lower and constantly falling rate. Heart examination reveals the same abnormalities together with murmurs and evidences of dilatation, and here the personal equation of the examining physician has played a considerable part in their interpretation. Accurate deductions cannot be drawn at present as to the severity of the lesions from the murmurs, and it is the author's personal opinion that dilatation has been diagnosed too frequently, though it would be wrong to say that it is unusual.

A sign of mild cardial disease of greater value on account of its constancy is the alteration in character of the first sound of the heart, consisting in the more or less complete disappearance of the muscular element of the first sound, making it weak and short, and what is usually called "valvular" in quality. Studies in regard to blood-pressure are incomplete and unsatisfactory. It is generally somewhat subnormal and when below 75 mm. always means a serious condition and below 70 mm. great danger. A progressive fall should excite more concern. General symptoms, such as pallor, apathy or irritability and vomiting, are often much in evidence. Loss of weight is common even in convalescence. The cause of death has not been determined by experiment, but the clinical evidence is conclusive that it is due to myocarditis. J. Howland (Jour. Amer. Med. Assoc., Dec. 19, 1908).

Case of diphtheria, with full heart block. The *a-v* bundle and node were found by the authors to be involved in an acute inflammatory process, and similar lesions were present in the *a-v* bundle in a case of malignant endocarditis in which conductivity was defective. In 3 cases of acute endocarditis, with nodal rhythm, the *a-v* node was acutely inflamed, the bundle being only and but slightly affected in one instance. Cowan, Fleming, and Kemaedy (Lancet, Feb. 3, 1912).

The writer studied serial sections of the heart in 15 children dying during or soon after an attack of diphtheria. Fatty degeneration was the most important change in the heart muscle, with hyaline degeneration of muscle-fibers. Fragmentation was rare. Intestinal myocarditis was found in 6 cases. Infiltration with leucocytes was present only as a symptom of the infection. In some cases the bundle of His showed fatty or hyaline degeneration, while the myocardium was nearly free from it, and *vice versâ,* demonstrating a certain independence pathologically of the atrioventricular bundle. The sudden paralysis of the heart in diphtheria may be due to pathologic changes in the myocardium or to essential lesions in the bundle. Tanaka (Virchow's Archives, Jan., 1912).

The blood shows a leucocytosis which is greatest during the height of the disease and decreasing during convalescence. The polymorphonuclear cells are chiefly affected by this increase. Myelocytes may be found in the peripheral blood, this being especially true in the severe cases, and they may range from 3 to 16 per cent. of the total white cells. There seems to be some relation between the severity of the infection and the degree of leucocytosis, but the leucocyte count is of little value from a standpoint of prognosis.

> Condition of leucocytes in diphtheria, before and after administration of **antitoxin** in 13 cases of clinically undoubted diphtheria. The writer found that diphtheria is attended by a varying degree of hyperleucocytosis, usually moderate. Occasionally hyperleucocytosis may be absent in extremely toxic or extremely mild cases. The differential counts in the leucocytoses of diphtheria show proportions of polymorphonuclear and mononuclear cells consistent with the grade of leucocytosis. In these leucocytoses the eosinophiles are present in unusually small numbers, and the myelocytes, basophiles in moderately small numbers. Neither the degree of leucocytosis nor the proportions of any of its constituent types of cells indicate, except within very broad lines, the severity of the infection or the outcome of the disease. The administration of **antitoxin** has no appreciable effect on the degree of the leucocytosis, the proportions of its constituent types of cells, or the staining reactions of these cells in dry preparations, stained either by Wright's method, Ehrlich's triacid mixture, or hematoxylin and eosin. Karsner (Univ. of Penna. Med. Bull., Sept., 1908).

The changes produced in the brain-cells of animals inoculated with diphtheria toxins have recently been made the subject of study (Carlo Ceni; Berkley). Swelling of the processes of certain cells of the brain with some minor changes in the conformation of the cells, but without evidence of degeneration of the cells or their processes, was observed. The cerebral were more affected than the cerebellar cells.

Various lesions have been found in the spinal cord in cases of diphtheritic paralysis, but none of the changes observed in the cord have thus far been accepted as the explanation of the paralysis.

Katz has recently reported finding, after careful examination of the cords of 3 fatal cases, distinct changes in the motor ganglion cells of the anterior horns of the cord. The changes were either a fatty degeneration affecting the cells or complete death of the cells with all processes, and especially the axis-cylinder. All ganglion cells of the cord were similarly affected, but not so markedly as the motor cells of the anterior horns.

The changes in the peripheral nerves, on the other hand, are looked upon by some as the most characteristic pathological lesion of diphtheria. The affected nerves are sometimes red and swelled, from congestion and edema, but the degeneration of the nerve-fibers is the characteristic feature of the process. Single nerve-fibers or a whole nerve-trunk may be affected. The changes may be either interstitial or parenchymatous. In the parenchymatous form there is usually a more or less marked infiltration of leucocytes within the nerve-sheath, between the sheath and the nerve-fibers, or between the fibers themselves. The medullary sheath of the nerve-fiber is swelled, undergoes a fatty degeneration, and may altogether disappear. The axis-cylinder undergoes a similar degeneration; it may be changed to a granular mass and be completely absorbed. The empty sheaths of Schwann may be the only evidence left of the former nerve-fiber. Sooner or later the degeneration stops; regeneration begins and usually results in complete restoration of the nerve-fibers. In the interstitial form the increase of the connective tissue of the endoneurium and perineurium is the marked feature of the process. In some cases the changes are both parenchymatous and interstitial.

The pulmonary changes produced by the experimental action of diphtheria bacilli or their toxins are slight and of no importance, but the pulmonary complications of clinical diphtheria are frequent, severe, and of great moment. Wright, More, Kanthack, Stephens, and others have demonstrated the presence of diphtheria bacilli in the lungs in fatal cases of diphtheria, but the presence of the bacilli apparently has but little to do with the production of pulmonary complications. In 1889, in an investigation of a series of 17 cases of pneumonia complicating diphtheria, Prudden and Northrup found streptococci both in the pseudomembranes in the throat and in the lungs. It was further shown that the inoculation of streptococci in susceptible animals served to produce changes in the lungs similar to those seen in clinical diphtheria. These observations have been fully corroborated, and the streptococci are accepted as the active agents in the production of the pneumonia which so frequently complicates diphtheria. Bronchopneumonia is met with in the great majority of fatal cases, especially in hospital practice. In the most acute cases we find the posterior parts of one or both lungs deeply congested, firm to the touch, and on section showing scattered areas of peribronchial consolidation, deep red in color. The lower lobes are usually more affected than the upper. In the slower cases we find the areas of pneumonia scattered throughout both lungs, but affecting the lower and posterior portions especially, the consolidation often involving a large part of both lungs and on section appearing mottled, reddish brown, and yellowish white. Pleurisy and empyema are rarely met with. In laryngeal cases with marked stenosis there is usually emphysema, both vesicular and interstitial. The interstitial emphysema may involve the cellular tissues of the neck and even extend over the trunk.

PROGNOSIS.—In no other acute infectious disease is the prognosis so uncertain as in diphtheria. Many factors must be considered in determining the prognosis in any given case:—

1. Age of the patient. Happily, children under 6 months of age are rarely attacked; but between that age and 2 years many cases are seen, and the mortality is often frightful. With increase in age the mortality falls steadily, but even in adult life diphtheria may readily prove fatal.

The following tables, taken from the article of Biggs and Guerard in "The Use of Antitoxic Serum," show the favorable influence of age very clearly:—

Herz:	Mortality Percentage.
0-1 year	80.00
1-3 years	45.00
3-5 years	40.00
5-10 years	17.00
Over 10 years	17.00

Baginsky:	Mortality Percentage.
0-2 years	63.3
2-4 years	52.8
4-6 years	37.9
6-10 years	24.6
10-15 years	14.6

Hirsch:	Mortality Percentage.
0-1 year	83.3
1-3 years	82.5
3-4 years	63.9
4-5 years	46.9
6-7 years	43.2
Over 7 years	22.2

The ratios are all derived from cases treated previous to the introduction of antitoxin or without its use. The analysis of a large number of cases treated by antitoxin, while the mortality ratios are diminished, shows that the age influence remains practically the same.

Age.	Cases.	Deaths.	Mortality percentage.
0-2 years	1494	469	31.4
2-5 years	3678	762	20.7
5-10 years	3184	473	14.8
Over 10 years	1444	99	6.9

Of 265 patients with phlegmonous diphtheria admitted to the Children's Hospital at St. Petersburg from 1895 to 1908, 67 died during the first day. The mortality decreased with the age, from 100 to 16.6 per cent. Early vomiting is an unfavorable sign, generally being followed by paralysis of the heart. Nephritis was observed in nearly all the cases from the first, but it proved mild. Under **antitoxin** the throat cleared by the beginning of the second week, but the heart symptoms generally developed at this time. Blumenau (Archiv f. Kinderheilkunde, Bd. lv, Nu. 5-6, 1911).

2. The site of the disease. Involvement of the larynx either primarily or secondarily adds greatly to the danger of the case. The large death rate under 2 years is due, in great part, to the strong tendency of the disease to invade the larynx during that period.

The use of **antitoxin** has materially changed all the figures relating to the fatality of the various forms of diphtheria, but the laryngeal process remains the most deadly.

3. The time of beginning treatment. In the use of antitoxin it has been demonstrated beyond the shadow of a doubt that, the earlier the remedy is employed, the surer is recovery, while after the fifth day the remedy exerts little or no influence.

It has always been quite evident that delay in undertaking treatment led to unfavorable results, but the vital necessity of promptness has been impressed upon us by the overpowering evidence afforded by the results obtained when antitoxin is resorted to early in the case.

The high mortality from this disease in the United States is due to the following factors: 1. Late diagnosis, late or inefficient prophylactic measures, lack of faith in **antitoxin,** and insufficient dosage in serious cases. 2. Cases diagnosticated early demand from 3000 to 5000 units immediately, to be followed by a further administration of 5000 units or more in from four to six hours if there is no improvement. Cases diagnosticated late, or those of a serious laryngeal character, or those showing especially toxic symptoms as indicated in the general condition of the patient and in the quality and rate of the pulse, should receive from 10,000 to 30,000 units immediately, and this dosage should be repeated at intervals of four to six hours until there is a complete subsidence of symptoms. 3. All of those in contact with diphtheria patients, or those suspected of such contact, should be given at once an immunizing dose of 1000 units of antitoxin. 4. All statistics indicate that there is no danger to the heart, kidneys, or nervous system from very large doses of antitoxin. The danger to the patient lies in using insufficient **antitoxin.** He injects it into the abdomen of children. Meddlesome therapeutics is extremely dangerous. Hill (Med. Rec., April 1, 1911).

4. The degree of toxemia. This feature is usually developed in proportion to the lapse of time from, and the severity of, the onset of the disease. It may be slowly or rapidly developed, and in many cases apparently mild in the be-

ginning we may later see the severest types of toxemia.

> Severe epidemic of diphtheria in Rostock, which began in September, 1911, totaling in four months 265 cases with 20 fatal, thus giving a mortality of 7 per cent. The writer compares this epidemic with the epidemic of 1905, which from June, 1905, to February, 1906, showed 210 cases, with a mortality of 5.2 per cent. The year 1906 had 377 cases, with only 5 per cent. of mortality; 1907, 415 cases, with 3 per cent. of mortality; morbidity and mortality slowly receded during 1908 up to 1911, in which year the month of August had 11 cases with no mortality. It showed the influence of a mixed infection, such as scarlet fever and diphtheria, and as sequelæ, necrotic processes leading to sepsis. Lux (Med. Klinik, Feb. 25, 1912).

5. The extent of the membrane and the rapidity of the extension.

6. The presence of complications, especially from bronchopneumonia or nephritis. The pneumonia of diphtheria is by far the most important of the complications.

> Mild diphtheria seems to exert little or no harmful influence upon the pulmonary lesion in the tuberculous. The antitoxin in small or large doses seems to have little or no effect upon the pulmonary tuberculosis. Immunizing doses may be given to patients with fever. Complications seem to occur after diphtheria no more often, possibly less, in the tuberculous than in the non-tuberculous. Brown, Allen, and Lupton (Amer. Jour. Med. Sci., Feb., 1907).

The late onset of the cardiac complications of diphtheria is to be remembered. No case of severe diphtheria can be considered altogether out of danger for some weeks after apparent recovery.

7. The surroundings of the patient. The mortality of diphtheria is considerably greater in hospitals or asylums for children than in private or dispensary practice. The crowding of the children together seems to exert a very unfavorable influence by exposing them to danger from complications, and most especially to pneumonia.

8. The mortality of diphtheria may vary greatly from year to year in the same place or in different epidemics, the causes of the variation not being apparent. Such variations in the type of the disease may properly be taken into account in the prognosis of individual cases.

> There are certain cases of diphtheria in which a fatal ending can with certainty be predicted. The symptoms presented by these patients are as follows: 1. A grayish color of the face, which in addition presents an anxious expression. 2. Vomiting. This seems independent of food and is not accompanied by nausea. It presents a similarity to cerebral vomiting. The vomited matter is yellow or green. 3. Abdominal pain. This is sometimes very severe. It is, however, nearly always present in these cases. It is referred to the umbilicus. No abdominal tenderness can be elicited. 4. Albuminuria. This is generally present and often to a large amount (from one-sixth to a quarter). There are no tube casts. 5. Suppression of urine is the rule in these cases. 6. Alteration in the rhythm of the heart sounds. This appears after the vomiting has set in. One of the sounds of the heart is reduplicated, thus giving an imitation of the sounds to be heard when a horse gallops. The patients are generally very restless and consciousness is maintained until the end. The membrane on the throats in these cases is dark colored and the smell of the breath is most offensive. He reports 6 cases. **Antitoxin** had no effect, though 6000 units were generally given. Harris (Lancet, Sept. 28, 1907).

> Systematic investigation of the plantar reflex in cases of diphtheria. The occurrence of Babinski's sign in diphtheria was first recorded by Kiroff in 1905, and since that time the writer has drawn attention to its frequency in association with precocious paralysis of the palate

and with hemorrhagic diphtheria. He now records his observations on 877 cases of the disease in which he has examined the state of the plantar reflex. An extensor response of the great toe, with varying movements of the other toes, was found in 172 cases—that is, in 19.6 per cent.; in 29 flexion alternated with extension, and in 676 the normal flexor response was obtained. It occurs in the acute stage and is replaced by flexion during convalescence. It is more frequently observed in the severe forms of diphtheria than in the mild ones, and its occurrence may have a certain prognostic value, although it is not of such grave omen as precocious paralysis of the palate. J. D. Rolleston (Review of Neurol. and Psych., July, 1910).

PROPHYLAXIS.—In typical diphtheria we have to deal with an acute infectious disease in which we now know the nature of the contagion and its ways of spreading. The bacilli present in the nose or throat of the patients are the active agents, and anything which may, either directly or indirectly, be contaminated by the discharge from the affected surfaces may be the means of communicating the disease to others. The first step in prevention is, therefore, the **isolation** of the diphtheria patient. Suspected cases should be isolated as thoroughly and promptly as those in which the diagnosis is settled. It is to be remembered that during epidemics or in any case of exposure many of the mild cases of "sore throat" are, in reality, diphtheria, and should be treated as such in this respect.

Moreover, as has previously been noted, diphtheria bacilli may be found in the throats of those who, although perfectly healthy, have been exposed to infection, these constituting the **carriers.** This is especially true of children, and in families where diphtheria is present the well children should be kept from attendance at schools or like gatherings, where they may possibly convey the disease to others more susceptible than themselves. In the course of epidemics it is often necessary to close all schools before the ravages of the disease can be controlled. A number of measures have recently been proposed to rid the carriers of these contaminating germs, but so far none has proven absolutely dependable.

Satisfactory results were obtained in Bremen by the co-operation of the authorities and the public in arresting the spread of diphtheria. Tests as to the ubiquity of the diphtheria germ always resulted negatively. Cultures made from the throats of 233 children and 72 adults brought to the hospital for various other affections never revealed the presence of virulent or even weakly virulent diphtheria bacilli. On the other hand, bacilli carriers were frequently encountered in the environment of diphtheria patients. The sick are divided into two classes, those of merely local or family importance and those important for the health of the public, as in case of a shopkeeper's family, a teacher or the like. All the inmates of the house in the latter class are examined for bacilli and, when found, the carriers are isolated and the rooms disinfected. The **isolation** has to be kept up for each carrier until no further cultures develop from their throats and the apartment is disinfected. In cases of the first class, the children of the family are kept away from other children until bacteriological examination is negative for each. Tjaden (Deut. Archiv f. klin. Med., Bd. lxxxix, Nu. 1-4, 1907).

Diphtheria bacilli often lurk in the recesses of the tonsils long into convalescence, and the writer has succeeded in freeing 13 patients from them by **crushing the tonsils,** thus squeezing out the plugs and secretions. He did this from one to nine times in the different cases, finally freeing the diphtheria convalescents in this way in from seventeen to thirty-eight days after the commencement of the disease. The results were promptest with the more accessible tonsils. Kretschmer (Med.. Klinik, Jan. 15, 1911).

The most persistent carriers were nurses, who at no time gave clinical symptoms. At about the height of the epidemic, on the recommendation of N. M. Haris, of Chicago, a spray of broth culture of **Staphylococcus pyogenes aureus** was used as a means of ridding the throats of the diphtheria organism. This method was tested in 8 cases, all carriers. A twenty-four-hour-old bouillon culture was sprayed into the nose and throat two or three times daily, all other treatment being stopped. In no instance did any harmful condition develop as a result of the introduction of the staphylococci. Two nurses, previously persistent carriers for days in spite of all antiseptic measures, failed to give one positive diphtheria culture after the first application of the staphylococcus spray. Three nurses, each having had one positive culture previous to the use of the spray, were constantly negative thereafter. One nurse had one positive culture after using the spray, and one other had three positive cultures after employment of the spray and then became negative. The eighth nurse was persistently positive in spite of, as supposed, the daily use of the spray; but it was later discovered that she had evaded using it as directed. More careful control of her use of the spray immediately cleared her throat of all diphtheria organisms. Apparently no harm results from the application of the spray. Catlin, Scott, and Day (Jour. Amer. Med. Assoc., Oct. 28, 1911).

While the number of cases of diphtheria has shown a gradual decline in the last five years, from 1302 to 578 cases, other infectious diseases have rather increased in frequency. In prevention of the spread of diphtheria, great stress is laid on convalescents still harboring the bacilli and they are kept under a certain supervision, and are not allowed to return to school or have anything to do with the traffic in foodstuffs. After recovery each one is examined at least once, school-children several times. The final disinfection of the premises follows the certification that no diphtheria bacilli are to be found in the patient's throat. It does little good to give the final disinfection while the patient is still scattering the bacilli. On re-examination of 2812 children who had had diphtheria, the bacilli were found in 312 on the second examination; in 100, on the third; in 7, the sixth; in 1 each up to the thirteenth, and in 2 on the fifteenth examination. Only 6 of the total 2812 thus had to be kept out of school for four weeks or longer. Drigalski (Berl. klin. Woch Sept. 16, 1912).

From the last of November, 1910, until August, 1912, all **fumigations** with data made by the Boston Board of Health were kept by one of the authors, who recorded any subsequent cases from that address together with the elapsed time. During this time 2675 fumigations were made after diphtheria with 48 "secondary" cases or 1.8 per cent. and 1748 fumigations with 27 repeat cases or 1.5 per cent. after scarlet fever. New cases after the fumigations following diphtheria: Four occurred during the first three days and a total of 19 during the first week; of this number 15 were sent to a contagious hospital and the fumigation performed within forty-eight hours of the time of the report of the case, consequently the new case had the exposure to either the same source of infection or the first case itself within nine days preceding the report of the new case. Therefore, it would seem quite probable that contact would be more apt to be the cause of the infection than the room which the patient occupied during the short period between the onset of the disease and his removal. The other 4 cases followed the release of the patient from quarantine after two successive negative cultures on different days, and it is a well-known fact that even this does not absolutely rule out the presence of organisms in the nose or throat. During the second, third, and fourth weeks there were but 16 "repeat" cases and of course exposure has been possible during this time. Over four weeks there were 13 cases from thirty-three to fifty-eight days, but the authors doubt very much if many would consider that these were due to infection from the room.

The "secondary" cases after fumigations following scarlet fever occurred as follows: 2 within the first three days, a total of 12 within the first week, 8 during the second, third, and fourth weeks, and 7 over four weeks, a total of 27. Of the 12 during the first week the room was fumigated within forty-eight hours of the report of the case in 9 instances, on the third day in 1 and after convalescence in the other 2. Of the entire number 19 were fumigated within forty-eight hours of the report of the case, 2 on the third day, 1 on the tenth day and 3 after convalescence. The number of "secondary" cases is raised by having 5 children in one family taken as follows: Dec. 4, 1911, fumigated the same day; Dec. 7, fumigated the eighth; Dec. 8, fumigated the twelfth; Dec. 15, fumigated the same day and the last one on the nineteenth. The authors believe that it seems very reasonable to assume that these infections came from persons rather than from inanimate objects. In order to demonstrate the fallacy of fumigation the board has since July 4, 1911, authorized the use of practically no disinfection after diphtheria and scarlet fever, using for each room, no matter what its size, a fumigator which would disinfect not over 500 cubic feet, and it can readily be seen that when this is used in rooms of from 1000 to 3000 cubic feet no real disinfection would be accomplished. The householders were instructed thoroughly to air the room following the "fumigation" and to wash all woodwork. The results have borne out the contention that fumigation after these infections was unnecessary, 63 per cent. of the secondary cases occurring with the smaller amount of fumigation which comprised 57 per cent. of the total number after diphtheria, and, if we except the family detailed above, 59 per cent. of the secondary cases of scarlet fever after the smaller amount of fumigation comprising 61 per cent. of the total number. If the labor of fumigation after diphtheria and scarlet fever would be dispensed with as it has been in many places after measures, and real disinfection carried on after tuberculosis, it seems to the authors that much more good would be accomplished and the public would then realize that it is the individual that is the cause of the spread of the acute infectious diseases in the great majority of cases. Arms and Whitney (Jour. Amer. Med. Assoc., from Amer. Jour. of Public Health, Oct., 1912).

Treatment of 17 cases of diphtheria by the **staphylococcus spray.** Six patients were subjects of active diphtheria, 3 were carriers pure and simple, never having shown local or constitutional symptoms of the disease. Almost invariably bacteriological culture of the throat secretions was negative after 6 or 8 applications of the spray, using a combined nasal and throat spray at four-hour intervals on two succeeding days, the first swab for examination being made on the third day. The preparation used was a fresh suspension of *Staphylococcus pyogenes aureus* in normal saline solution, or a bouillon culture twelve hours old, the spray being kept at a temperature of 96° F. Sufficient is used to make the pharynx dripping wet, and the nasal cavities are sprayed until the liquid runs down the back of the throat. Pure cultures of the staphylococcus will cause a disappearance of diphtheria bacilli when sprayed into the throat and nasal cavity. He finds the treatment most effective in those who are carriers pure and simple. Lorenz and Ravenel (Jour. Amer. Med. Assoc., Aug. 31, 1912).

The discouraging results obtained from the use of the usual methods in cases of diphtheria bacillus carriers render more active measures necessary. Two cases of persistent Klebs-Löffler bacillus, in which the throats were swabbed with fresh broth cultures of **Staphylococcus pyogenes aureus** every morning by the writer, and the remainder of the culture placed in an

> atomizer to be used as a **spray** in the throat by the patient, every two hours during the day. A fresh culture in both is made each morning, no culture over twelve hours old being used. By this treatment the desired results were obtained in days instead of weeks. It should be used during convalescence even though all signs of active inflammation have disappeared. Bell (Lancet-Clinic, Aug. 31, 1912).
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> The writer found spraying of the throat and nose of the diphtheria convalescent with fresh cultures of the staphylococcus effective when applied every three hours. The cultures must be fresh and living if success is to be secured. The result was the rapid disappearance of the Klebs-Löffler bacilli from the throat and nasal passages and the hastening of convalescence. In the carrier cases similar results were obtained by removing the organisms from the nasal and oral cavities. Wiener (N. Y. State Jour. of Med., Feb., 1913).

The past few years have been marked by the establishment in our large cities of a system of inspection by trained physicians of all school-children who present the first symptoms of illness: a progressive step in preventive medicine that will undoubtedly do much to protect these communities from epidemics of diphtheria. Suspected cases of diphtheria are to be isolated, but should not be put into diphtheria wards or hospitals until the diagnosis is assured. Our reliance must be upon the bacteriological diagnosis, for in case of exposure the mildness of the individual case is no surety that it is not dangerous to others.

These cases call for especial care, both in making and in examining the cultures. With proper methods twenty-four hours should suffice to settle the question of diagnosis. In case of doubt the isolation of the patient should be continued and the bacteriological examination repeated.

In all our large cities provision is now made for the treatment of diphtheria in special public hospitals. To these hospitals are sent all cases that cannot be properly cared for and isolated at home.

Proper **isolation** of diphtheria cases developing in hospitals or asylums, especially those for children, is of very great importance, since these institutions contain the most susceptible material for the action of diphtheria bacilli. They should be provided with diphtheria wards, located, if possible, in separate buildings. The isolation of such wards should be complete. In no other way can the inmates of such institutions be protected from repeated outbreaks of diphtheria.

In private houses one or more rooms should be set apart for the use of a diphtheria patient. No one but the patient and the attendants should be allowed to enter the sick-room. All expectoration, bits of membrane, etc., should be received in cups containing a solution of **carbolic acid**, 1:40, or **bichloride of mercury**, 1:1000. Instead of handkerchiefs, bits of gauze or old linen should be used, and burned when soiled. All bedding and clothing used during the attack should be soaked for several hours in a 1:40 solution of carbolic acid and afterward boiled. All eating utensils should be sterilized by boiling. Nothing that has been in the room should be taken from it without subjecting it to sterilization in some way.

The physician in charge of a case of diphtheria before entering the sick-room should cover his clothing by a cotton or rubber gown reaching to the feet and a cap to completely cover the hair. The cap and gown should be kept outside the sick-room and should be sterilized at the conclusion of the case. The physician should remember that, in examining the throat in cases of diphtheria, he stands in great danger of infection by having the patient cough in his face. Many a life has been sacrificed by careless exposure in this way. As a measure of protection, the physician is often advised to have a pane of ordinary window-glass held before the patient's face during inspection of the throat.

Unfortunately, very few men willingly adopt a cumbersome device which at the same time interferes with the examination; but, in case the patient does cough during the examination, the physician should protect himself by thoroughly washing the face and hair with soap and water, and then using a solution of **bichloride**, 1 : 1000. The hands should always be washed and disinfected on leaving the patient's room.

Nurses caring for diphtheria patients should especially avoid contracting the disease by exposing themselves to the discharges from the nose or throat of the patient. Practically there is no danger from the breath of the patient. The nurse should keep her hands thoroughly clean at all times and should have a disinfecting solution of **carbolic** or **bichloride** at hand so that she may use it constantly. A cleansing gargle of **normal salt solution, Dobell's solution,** or **Seiler's solution** should be used several times a day. It is advisable to administer an immunizing dose of **antitoxin** to all persons exposed to the disease, and 500 to 1000 units are sufficient for this purpose.

If this is not done, **antitoxin** in protective dose should be given at the first sign of a "sore throat."

After leaving a diphtheria case the nurse should thoroughly disinfect both her clothing and her person. It is also customary to require the nurse to allow a period of at least five days to pass after leaving a case of diphtheria before assuming charge of any other patient.

Length of Quarantine.—The bacteriological researches of recent years have given us some very definite information bearing on this point. It has already been noted that the bacilli may persist in the throat for weeks after an attack, and that such bacilli have been proved fully virulent. Park reports a series of careful observations upon the time of the disappearance of the bacilli from the throat in 1736 cases of diphtheria. Briefly, he found that the bacilli had disappeared within one week in 3 per cent. of the cases, in one-third of the cases at the end of the second week, in two-thirds at the end of the third week, in four-fifths at the end of the fourth week, and in the remainder the bacilli persisted for varying periods up to 91 days. This last case was one of simple nasal discharge containing diphtheria bacilli, from which both nurse and mother contracted diphtheria. The mildness or severity of the case gives no basis for determining the time that the bacilli may remain in the throat. The only accurate method of determining the period of quarantine is that of making cultures from the throats. Only when cultures fail to show the presence of the bacilli in the throat or nose can the case be regarded entirely devoid of danger to others. If cultures cannot be employed, we may elect an arbitrary period of three weeks from the disappearance of membrane for the removal of quarantine restrictions. After that time, if the bacilli have not actually disappeared from the throat, they are but few in number, and the danger of communication is slight.

Disinfection of the infected rooms upon the termination of the case should be thorough. The walls and ceilings are to be scrubbed with **bichloride,** 1:1000, or rubbed down carefully with bread: a simple method of removing the clinging dirt and bacteria by mechanical means. The woodwork, floor, and furniture are to be scrubbed with bichloride The woodwork, walls, etc., are to be repainted or papered anew. Carpets, upholstery, etc., can be disinfected by steam. Clothing, linen, etc., may be boiled. Anything which cannot be disinfected by some of these means should be burned. Books and toys that children have used during their illness should be thus destroyed. Even the most careful disinfection will, in some cases, prove ineffective. The following are the regulations for fumigation established by the New York Board of Health:—

"All the crevices in rooms to be fumigated must be sealed or calked to prevent the escape of the disinfectant, and one of the following disinfectants used in the quantities named:—

"(*a*) **Sulphur,** 4 pounds for every 1000 cubic feet of air-space, eight hours' exposure.

"(*b*) **Formalin,** 6 ounces for every 1000 cubic feet of air-space, four hours' exposure.

"(*c*) **Paraform,** 1000 grains for every 1000 cubic feet of air-space, six hours' exposure.

Apart from these measures with respect to the cases already developed, much may be done to prevent the spread of diphtheria by properly caring for children who may be exposed to infection. Catarrhal conditions of the nose and throat undoubtedly afford a favorable soil for the location and growth of diphtheria bacilli. Enlarged tonsils and adenoid growths in the nasopharynx fall in the same category. All such conditions should be carefully treated.

Healthy mucous membranes are a safeguard against attacks of diphtheria.

Immunization by Injections of Antitoxin.—By the injection of small doses of antitoxin it has been found possible to induce an artificial immunity which holds good for a period of at least four weeks, as a rule. Epidemics of diphtheria in children's hospitals or asylums have been repeatedly checked by protective injections of antitoxin in all the children exposed.

In the article on the "Use of Antitoxin," by Biggs and Guerard, previously quoted, a summary of thirty-five reports covering 17,516 injections of antitoxin for the purpose of immunization is given. Following these injections 131 cases of diphtheria developed, 109 mild cases and 1 fatal case within thirty days of the date of injection; 20 mild cases and 1 fatal after thirty days. The writers state that "the duration of immunity after injection has not been definitely determined and undoubtedly varies. Some hold the opinion that it lasts only one or two weeks, others that it extends over thirty days or more. Four weeks may probably be considered as the average duration." The results certainly justify the further trial of this method of protection.

Prophylaxis should include isolation of every patient with an affection in which the Löffler bacillus is recognized as the cause. **Isolation** should be continued until negative results are obtained in two bacteriological examinations with an interval of a week at least. If the positive findings persist after forty days of convalescence the patient can be dismissed, but the health of persons in his environment must be supervised. Roussel and Job (Revue de méd., vol. xxv, No. 7, 1906).

In the course of an epidemic over 400 immunizing doses of **antitoxin** were given to 129 tuberculous and 45 nontuberculous individuals. In no case did any infection occur. In 4 instances diphtheria developed between the fourteenth and sixteenth days following the first injection, and in 1 case four days and in another one day after the second injection. The authors state that in the presence of diphtheria epidemic patients with pulmonary tuberculosis should be treated as regards the diphtheria like otherwise healthy individuals. Brown, Allen, and Lupton (Amer. Jour. Med. Sci., Feb., 1907).

Antitoxin injected to protect children with measles against diphtheria proved disappointing. The injections failed to immunize the infants or to modify the severity of the disease. Of 1178 children in the measles wards treated with antitoxin, 2.12 per cent. developed diphtheria in the first week, 2.04 in the second, 0.51 in the third, 0.26 in the fourth and 0.17 per cent. after the fourth week. The corresponding percentages for the 1156 children not injected were smaller, being, respectively, 1.56, 1.73, 0.52, 0.78, and 0.43 per cent. The mortality averaged 36.6 per cent. in the first group, and 32.3 in the second. Markuson and Agopoff (Arch. de méd. des enfants, May, 1911).

In a series of 348 children with measles or scarlet fever all were given prophylactic injections of 500 or 600 **antitoxin** units as soon as they entered the contagious disease ward, and the injection was repeated each two weeks afterward. Nineteen of the children, that is, 5.5 per cent. developed diphtheria later, and signs of serum sickness were evident in 18.4 per cent. As these results were not considered satisfactory, the writer devised a method of inducing active immunization which seems to be promising. A wad of cotton impregnated with **diphtheria toxin** was introduced into each nostril alternately for an hour each day for ten days. In experiments on adults and on 17 children it was found that there was marked production of antitoxin by this method. Experimental research indicates that the immunity thus acquired may last for months and years. The method may perhaps be advantageously combined with passive immunization by injection of antitoxin when rapid action is desired. The diphtheria toxin was diluted with twice the amount of salt solution in a later group of 11 children to avoid by-effects, and the tampon was left in the nose only half an hour every third day. Blumenau (Jour. Amer. Med. Assoc., from Jahrbuch f. Kinderheilkunde, Aug., 1911).

Increasing the dose of **antitoxin** beyond a certain point does not further lower the mortality, which, during a recent epidemic, was about 18 per cent. On the other hand, the results of immunization of those who had been or were to be exposed were brilliant. Of nearly 500 so immunized, but 5 developed the disease, and that in a very mild form. Of the small number in which immunization was refused 14 developed the disease with 3 deaths. Eckert (Deut. med. Woch., Nov. 21, 1912).

At least three weeks of immunity are conferred to a certainty by means of **antitoxin**; in individual cases it may be prolonged, say up to three and four months. If new cases develop during this period they are extremely mild. In regard to anaphylaxis, it has become a bugbear with many institutional physicians because it antagonizes the idea of prophylactic injections. They often prefer to reserve the first injection until the disease has actually been contracted. The writer has met no anaphylaxis in his practice after a single prophylactic injection. It is only to be feared when in the course of a year a number of injections are given at considerable intervals. Braum (Deut. med. Woch., Feb. 6, 1913).

ACTIVE IMMUNIZATION BY INJECTIONS OF MIXED TOXIN AND ANTITOXIN.—Von Behring has recently worked out a method by which a prolonged, active immunity to diphtheria may be produced. It consists in injecting a combination of of diphtheria toxin and antitoxin so proportioned that upon administration to guinea-pigs the antitoxin almost or quite offsets the poisonous action of the toxin. In human beings such a mixture, though bringing about prolonged immunity, causes only a slight reaction, provided the system has not already become oversensitive to diphtheria bacilli.

An important additional result is that in patients sensitive to horse serum a passive immunity can be produced by injecting antitoxic serum obtained from human beings; furthermore, this immunity will not rapidly disappear, as would be the case were horse serum used, but will persist as long as the active immunity obtained with the toxin-antitoxin mixture, owing to the fact that the material introduced is derived from an individual of the same species.

Children from 4 to 15 years old are almost always more sensitive than the newborn to the toxin-antitoxin mixture. Thus, with a dose which in a newborn infant would cause practically no reaction, it was found that in an older child the same amount (1/16 c.c.) caused an intense febrile reaction, with the active production of antitoxin by the body to the extent of 600,000 units. Since this is far in excess of the intensity of immunity required for practical purposes, there is ample opportunity for producing a sufficient degree of protection without inducing a marked reaction. In the child referred to it was calculated, from several observations of the antitoxic power of the blood, that it would take over two years before this power would diminish to a level which is attained with the ordinary passive immunization by diphtheria antitoxin in ten days.

The toxin-antitoxin mixture used must be free of aërobic and anaërobic germs, and must be non-toxic in guinea-pigs in the dose of 0.0005 Gm. for every 100 Gm. of body weight. Infants are to be given 0.0001 Gm. as the initial dose, and older children only 0.00005 Gm., injected under the skin in 0.001 Gm. of fluid. The classes of subjects to be inoculated are those exposed to diphtheria in hospitals, schools, and buildings occupied by several tenants; well persons, not exposed to diphtheria at the time, in orphan and insane asylums, prisons, etc., and diphtheria carriers—the latter being usually very sensitive to the remedy and developing a high degree of immunity. In beginning cases of diphtheria and in persons with a weak heart and irregular pulse the mixed inoculations are not at present to be tried.

The safety of the toxin-antitoxin mixture has been proved, and its efficiency in producing active immunity was illustrated by experiences in Hagemann's ward in Marburg, where none of the children treated were attacked with diphtheria or harbored the bacilli, in spite of the fact that "carriers" were constantly present and an epidemic of the disease actually took place in the ward. An important feature of the method is that it may permit of elimination of the danger attending diphtheria carriers. Von Behring (Semaine méd., May 7, 1913; N. Y. Med. Jour., June 7, 1913).

GENERAL MEASURES.—First of all, the sick-room should be well lighted and ventilated. Care in this respect is especially necessary in children's hospitals. Crowding a number of cases of diphtheria together in one ward is undoubtedly harmful. It is much better to have a number of small wards, accommodating three or four patients, than one large one in which all are assembled together. Cases in which pneumonia has developed should not be kept in the room with those still free from it. Attention should be given to feeding the patients, as the best means of enabling them to bear the attack of the disease upon the vital powers. Usually, on account of the soreness of the throat, fluid foods can be best taken, but semisolids can be given in some cases. Our chief reliance must be upon milk. It should be given at regular intervals, every two hours, and in such quantity as the patient will take. There is little danger of overfeeding. The difficulty is usually to get the children to take sufficient nourishment. In addition to the milk, we may give beef-juice, beef-tea, or thin gruels. In children that have been intubated semisolids can sometimes be taken better than fluid nourishment. Bread and milk answer the purpose in such cases.

Nursing children should be fed with milk drawn by a breast-pump. In this way the children are saved the exertion of suckling and the mothers are protected from the danger of infection.

In septic cases the children often refuse food altogether or vomit it immediately it is taken. They may then be fed by the stomach-tube. If the tube cannot be passed through the mouth, we can usually succeed in passing it through the nose. This method may also be employed in intubated cases where the attempt to swallow food is followed by violent coughing or choking.

Rectal feeding with peptonized milk is a last resort, and seems to be of little value in children.

Rest in bed is an essential feature of proper treatment. Whatever handling or interference is required should be so arranged as to tax the patient as little as possible. Zeal for thorough local treatment has often led to fatal excitement and exertion on the part of the patient. Especially in cases of cardiac weakness should absolute quiet be enjoined, and all treatment that tends to excite the child or cause it to struggle avoided. **Opium** or **morphine** may be used to insure quiet under these circumstances.

Steam inhalations have long been employed for the purpose of increasing the secretions of mucus from the mucous membranes, softening the diphtheritic deposits, and hastening their separation. The **croup-kettle** has almost become a household utensil. To increase the efficacy of the steam, **carbolic acid, turpentine, eucalyptol,** and other aromatic antiseptics have been added to the boiling water. These measures are indicated in the cases of diphtheritic laryngitis before the antitoxin has had time to act and when the respiratory distress is not sufficiently great to warrant intubation. Here the inhalation of steam gives temporary relief. The tent should be arranged to allow ample ventilation, as otherwise the process may be very exhausting and do more harm than good. The child should not remain under the tent longer than fifteen minutes, and the treatment should not be repeated oftener than every three hours. In many cases the inhalation of steam as it comes from the kettle, without the use of a tent, is sufficient.

LOCAL TREATMENT.—In certain cases the local treatment in diphtheria is of importance.

The object sought in such treatment has changed considerably within recent years. We no longer seek to remove the membrane by local applications or by mechanical means, nor do we expect to destroy the bacilli in the throat. Experience has taught us that we can get rid neither of membrane nor of bacteria by local treatment, and also that too energetic efforts to accomplish these ends do harm instead of good. We have, therefore, abandoned the mechanical removal of the membrane, the application of destructive powders or solutions to it, and the use of strong antiseptics to the affected parts. We endeavor simply to keep the nose, mouth, and throat clear of the secretions which may either obstruct them or by their decomposition and absorption increase the toxemia.

In the milder types of pharyngeal diphtheria no local treatment is necessary, the antitoxin being sufficient. In these cases, with the use of a sufficient amount of **antitoxin,** the general symptoms are very quickly relieved, the pain disappears, and the membrane is cast off. In the severer cases and in those with mixed infections, where there is great pain and when foul secretions accumulate in the mouth and pharynx, local treatment is of great value. The best method is to use the solution as an irrigation, and the best instrument for this purpose is an ordinary **douche bag.** The fluid should be non-irritating, and **normal saline, Seiler's fluid,** or a saturated solution of **boric acid** can be used. The patient should be in a horizontal position, lying on his side, and, if a child, wrapped in a blanket to control the arms and legs. The flow should be interrupted every few seconds to give the patient an opportunity to recover his breath. It is very important that the solution used be very hot, as the heat is of great value in relieving the pain. If the child struggles against the treatment to the point of exhaustion it should be abandoned, but, as a rule, even the smallest children become accustomed to the irrigations and rather welcome them for the relief they give. The irrigations can be given from every two to every six hours, according to the severity of the disease.

In the majority of cases of nasal diphtheria local treatment is unnecessary, and, if not carefully given, nasal irrigations can do much harm. Certainly the incidence of otitis media is less without the use of nasal irrigations and douches. In certain of the severe cases where there is a profuse nasal discharge and great difficulty in breathing, douches are of service, but the fluid should be allowed to run into the nostrils under small pressure, always remembering the relatively large size and patency of the Eustachian tubes in infants and small children. In many instances it is sufficient to pour the fluid into the nostrils from a spoon. The solutions recommended for pharyngeal irrigations are the best to use in the nose.

Where there is much swelling of the cervical lymph-nodes, **hot or cold applications** may be used. Heat is preferable in infants; in older children the **ice-cap** may be used. **Flannel pads** or **spongiopilene wrung out of hot water,** or **poultices,** may be used in the former case.

> Local treatment in diphtheria the writer believes is quite as essential as the general treatment by antitoxin. Treatment may be by irrigation, nebulization, or painting. **Boric acid** (1 per cent.), **salicylic acid** (½ per cent.), **sodium chloride** (1 per cent.), etc., have been used by him, but the best results were obtained with occasional swabbing with **oxygen** solution (1 vol. perhydrol in 10 of water), followed by swabbing with a bivalent serum prepared for local use by Bandi. During the last twenty months the writer has carried out this type of local treatment in 691 cases of diphtheria; in some cases no serum was injected. The **Bahdi serum** is non-toxic, non-coagulating, and non-caustic, and causes the diphtheria bacillus to disappear more quickly than any other application. Probably the reason for its success lies in its very strong opsonic power. Appiani (Gaz. degli osped., Sept. 13, 1908).

The severe form of primary streptococcus diphtheria occurs oftener than we have been led to believe. Complications of suppuration of the cervical glands occur frequently, and complications of acute exudative nephritis occur in all severe cases and in some become chronic. In the treatment, he has found very little of any avail, except thorough toilet of the mouth and nose, with stimulation to tide the patient over the time until the toxemia subsides. Diphtheritic serum has been given even in large doses, up to 20,000 units without any effect. Antistreptococcus serum has also been given without effect. The only thing he has found of value is the spraying of the throat with **hydrogen peroxide, ice-bag to** the **neck,** and douching of the mouth and nose with **salt solution.** When the urine becomes scanty or suppressed, **hot rectal irrigations** or **hot-water bags to** the **region** of the **kidneys** are useful. Orgel (Med. Rec., Aug. 13, 1910).

Case in which, after antitoxin, throat cultures showed abundant diphtheria bacilli three weeks after start of disease. Repeated applications to the throat of a dilute culture of **Staphylococcus pyogenes aureus,** made by inoculating 8 c.c. of bouillon with a loopful of a fresh agar growth of the coccus, led to disappearance of diphtheria organisms from throat, thus preventing the child from being a "diphtheria carrier." General condition markedly improved. No untoward effects were observed. H. Page (N. Y. Med. Jour., Dec. 23, 1911).

GENERAL TREATMENT.—With the advent of antitoxin most of the remedies for diphtheria have passed from use. A few still occupy a position which warrants some attention. In the treatment of pharyngeal or tonsillar diphtheria the tincture of the **chloride of iron** has long been regarded as of great value. Jacobi commends its use, advising a daily allowance of 1 dram (4 Gm.) for a child 1 year old, 2 or 3 drams (8 to 12 Gm.) for children from 3 to 5 years old. It is to be given diluted with water and glycerin. He admits that it cannot be tolerated by some patients, and that **alcohol** is to be preferred in septic cases. Under present conditions its use must, therefore, be very limited.

In the treatment of laryngeal diphtheria the best results previous to the use of antitoxin were attained by the administration of **mercury.** The drug was given internally in the form of the bichloride, or the patient was treated by **calomel** fumigations. The **bichloride** was given in hourly doses to the amount of 1/6 to 1/2 grain (0.01 to 0.03 Gm.) in twenty-four hours, each dose being preceded and followed by copious draughts of water. This treatment was continued for from four to eight days, and good results were claimed for it.

Calomel fumigation was a more elaborate process. A tent or canopy was rigged over the patient's crib. Beneath this tent 15 grains (1 Gm.) of calomel were volatilized every two hours for two days and nights, then every three hours for the third day, every four hours for the fourth day, and thereafter three times a day, according to indications. The patients sometimes suffered from stomatitis and diarrhea and developed pronounced anemia; not infrequently the attendants were salivated; but this form of treatment gave better results in intubated cases than any other employed before the introduction of antitoxin.

Among other remedies that have been recommended, **pilocarpine, guaiacol, citric acid, sodium hyposulphite,** and **myrrh** have received the greatest attention; but the fact must be borne in mind that, in the majority of cases treated, the diagnosis has not been established by bacteriological examination.

Stimulants.—These are required in every case of diphtheria showing any marked degree of constitutional depression, most of all in septic cases. The pulse and the general condition of the patient are the guides in their administration.

> The writers have employed **formic acid** in 412 patients during 1906 at the Edinburgh City Hospital, with the result of diminishing the death rate by 1.8 per cent. over that of the previous year. Previously strychnine had been given as a heart tonic, but during 1906 formic acid in 25 per cent. aqueous solution, in doses of 5 to 20 minims (0.3 to 1.25 c.c.) every four hours, was substituted, the dosage being graduated rather by the severity of the infection than by the age of the patient. No change in the heart action was noted until after about forty-eight hours, and then the change was rather a negative one, that is to say, many of the severe infections did not show the expected cardiac weakness and irregularity; on the other hand, the pulse in many instances was much improved in character, as was the color of the skin and the general nutrition. Patients were observed who appeared doomed to die of heart-failure, but who rallied, this manifestation being attributable to the possible limiting effect of the formic acid upon the degeneration of the heart muscle or its beneficial action upon the undamaged muscular tissue. The most striking result of the treatment was the diminution of the number of instances of paralysis, the percentage being only 2.9, as against 9.09 in the previous year, which was the lowest in several years. Ker and Croom (Edinburgh Med. Jour., vol. vi, p. 487, 1907).
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> Effects of **diphtheria endotoxin** on 24 diphtheria patients of whom many had harbored the diphtheria bacilli for many weeks or months after the acute attack. After one or more injections all the patients showed definite improvement. In many the diphtheria infection ceased entirely; in some it persisted, and the patient remained uncured; but even in these unsuccessful cases they noted invariably a diminution in the number of bacilli.
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> Endotoxin is prepared by growing a virulent culture of diphtheria bacillus on serum or blood agar, collecting the growth, washing it two or three times in sterile physiological salt solution so as to remove the toxin, grinding the bacterial mass in the presence of intense cold, and filtration of the ground mass through a Berkefeld filter. The filtrate contains the endotoxin and is standardized by the addition of sterile salt solution so as to contain from 2 mg. to 5 mg. (1/32 to 1/12 grain) per cubic centimeter (16 minims). With regard to dosage, they first used the endotoxin in doses of from 0.5 mg. to 1.0 mg. (1/125 to 1/64 grain), but the patients did not do so well as when they gave an initial dose of 2 mg. (1/32 grain). At the end of a week or ten days, if the culture was still positive, a second injection of 5 mg. (1/12 grain) was given and this, if necessary, was repeated later. The dose was the same for children and adults. No ill effects, except some redness and tenderness around the site of injection, and in one case a transitory rise of temperature and a feeling of malaise followed the administration of the endotoxin. Hewlett and Nankivell (Lancet, vol. clxxxiii, p. 143, 1912).

The best of all stimulants is **alcohol.** A child of 3 or 4 years can take at least 1 ounce of whisky or brandy in twenty-four hours. It should be given diluted with from 4 to 6 parts of water. In the severe cases the quantity of alcohol may be increased to several times the amount named above. It is best to give it apart from the food, as the patient may decline to take the stimulant, and may be led to refuse the food because of its admixture. Next to alcohol, **strychnine** is of most value. The 1/100 part of a grain (0.00065 Gm.) may be given every two or three hours to an infant 1 year old; twice that amount to a 3-year-old. The drug may be pushed till the deep reflexes show an exaggeration. **Digitalis** and like cardiac stimulants may be called for by the condition of the heart, but most reliance is to be put in alcohol and strychnine.

To prevent heart-failure in diphtheria, **antitoxin** should be given at the earliest possible moment, and in large doses; 4000 to 6000 units should be the minimum dose, while in severe cases 12,000 to 24,000 units. The point next in importance to antitoxin is **rest**, both physical and mental. In the vast majority of the cases, after the first three weeks have passed, death from heart-failure will occur only as the result of some complication or strain. A slow irregular pulse is of bad prognostic significance. The patient should be kept with the head low, and disturbed as little as possible. Great care should be exercised in spraying the throat. Another danger lies in the strain produced by vomiting. Bolton (Lancet, Feb. 3, 1906).

The essentials of treatment for the heart condition accompanying diphtheria are: 1. Prompt and sufficient dosage of **antitoxin.** 2. **Rest** in bed not less than three weeks. 3. Attention to the condition of the abdominal viscera. 4. A nutritious, easily digestible **diet.** 5. Certain drugs, each according to the indications. For a slow heart, **atropine;** for a racing heart, **camphor,** and **ice to the precordium;** for vascular failure, **ergot.** 6. If the heart-failure is indicated to an overwhelming toxemia with lethargy, **hypodermoclysis.** Porter (Archives of Pediatrics, Aug., 1909).

The heart should be carefully examined daily in all cases of diphtheria, however mild they may appear to be, and a careful lookout kept for any of these danger signals. Prolonged and absolute **rest** in bed is essential when heart complications threaten, and on no account should the patient be allowed to sit up in bed. The **diet** should be carefully regulated, and small readily digestible meals should be given at from two and one-half to three hours' interval, as there is danger in overloading the stomach of upward pressure on the heart, which may arrest a weakly acting right ventricle and prove fatal.

Brandy and **strychnine,** in suitable doses, the latter administered hypodermically, are the best cardiac stimulants to administer, but they should be kept in reserve, and not exhibited too early in the disease. **Digitalis** is of more doubtful service, and must be employed with great caution, as it is more likely to do harm than good in cases of severe myocardial degeneration. Sir J. F. H. Broadbent (Practitioner, Jan., 1909).

The free use of **adrenalin** is beneficial in severe cases. One mg. ($\frac{1}{65}$ grain) in 1:1000 solution should be injected subcutaneously every hour or two, up to 10 or even 24 mg. ($\frac{3}{8}$ grain) daily. Kirchheim (Münch. med. Woch., Dec. 20, 1910).

The heart affection seems to be merely one manifestation of an insidious diphtheria intoxication. As the original diphtheria is subsiding after an apparently normal course, convalescence is suddenly interrupted by vomiting and the patient refuses all food, while motor agitation, even delirium, alternates with apathy; there is striking pallor and the pulse is soft and faint, although the heart findings are comparatively negative. This syndrome may follow an apparently mild diarrhea, but usually the disease is of a rather severe type. The vomiting and the psychic and vascular disturbances all point to mischief in the central nervous system, the result of the action of the diphtheria toxin. Treatment must be prompt and energetic, and for this the writer commends lumbar injection of **antitoxin** and reports some favorable experiences with it, although he was unable to save all his patients. Bingel (Deut. Archiv f. klin. Med., Bd. civ, Nu. 3-4, 1911).

The cardiac depression must be combated by the administration of strychnine, belladonna, and adrenalin, which gave the writer four successful cases, though, of course, he has also had his failures. The formula used is as follows:—

Atropine sulphate	1/100 gr. (0.00065 Gm.).
Strychnine hydrochloride..	1/100 gr. (0.00065 Gm.)
Adrenalin chloride solution (1 in 1000) ..	5♏ (0.3 c.c.).
Water	20♏ (1.25 c.c.).

To be administered hypodermically every four hours. Coghlan (Brit. Med. Jour., March 9, 1912).

The **antitoxin** treatment of diphtheria has been in general use the world over since 1895, and in that time has won for itself the right to be regarded as a specific.

Previous to 1894, when **antitoxin** was first employed, the mortality from diphtheria in all the Paris hospitals for children averaged 50 per cent. As compared with this the following statistics for the years from 1901, in Marfan's service, are peculiarly significant. By reduced mortality is to be understood that calculated after the exclusion of cases dying in less than twenty-four hours after admission. For 1901-02, 1122 cases, total mortality 21 per cent., reduced mortality 12.3 per cent.; for 1902-03, 1048 cases, total mortality 15.8 per cent., reduced mortality 11.1 per cent.; for 1903-04, 605 cases, 14.2 and 9 per cent.; for 1904-05, 561 cases, 7.6 and 5.47 per cent.; and for 1905-06, 534 cases, 10.11 and 6.97 per cent. Marfan (Revue men. des mal. de l'enfance, April, 1907).

Statistics on the effects of **antitoxin.** The writer divides the cases studied into two classes. The first class of cases comprise those treated before the use of antitoxin, and the second those treated with antitoxin. In 1087 cases of diphtheria belonging to the first class, the mortality was 37.8 per cent., while in 4226 cases belonging to the second class the mortality was only 9.7 per cent. A much smaller number of those patients treated with antitoxin require tracheotomy or intubation to relieve laryngeal stenosis. Thus, of 1087 patients admitted before the use of antitoxin, 605 required such operations, or 55.5. In comparing this with the antitoxin period he found that of 4226 cases, only 1231 required operations, a percentage of 29. Furthermore, the mortality in the cases operated upon is much lower under the use of antitoxin than before it was employed. Thus, in the 605 cases operated upon before antitoxin, 334 died, a percentage of 55.2, while of 1231 cases operated upon with serum treatment, only 330 died, or 26.8 per cent. Timmer (Berl. klin. Woch., Bd. xlvii, S. 1313, 1910).

The cases of diphtheria which have occurred during the past twelve years in Philadelphia, as reported to the Bureau of Health, numbered 43,997. Of this 7097 terminated fatally. With more extensive use of the diphtheria **antitoxin** the mortality has been reduced from 24 per cent. in 1898 to 12.1 per cent. in 1909. Mary Sallom (Med. Record, July 9, 1910).

The antitoxin is derived from the blood of horses that have been subjected to repeated inoculations of increasing doses of the toxins produced by the diphtheria bacillus. The course of treatment usually occupies several months. When immunity has been thoroughly established in a horse the blood is drawn from a jugular vein into sterilized vessels and allowed to clot. The clear serum is then siphoned off into small sterilized bottles, each of which contains sufficient antitoxin for one dose, and is preserved by the addition of camphor or carbolic acid in small quantity. The antitoxin thus prepared is a clear, limpid fluid, having the color of blood-serum. If kept in a cool, dark place, it remains clear and is efficient for several months. After a year it begins to lose some of its power. Often before this time the serum becomes turbid and is unfit for use. The strength of the serum is expressed in terms of an arbitrary unit, dependent upon its power to neutralize definite quantities of diphtheria toxins. An antitoxin unit, according to the standard established by Ehrlich, is the amount of antitoxin necessary to neutralize 100 times the minimum lethal dose of diphtheria toxin for a guinea-pig of given weight. Since the reaction of different horses to the diphtheria toxin varies, the number of units in each cubic centimeter of serum will vary. Upon each bottle of antitoxin is indicated the number of antitoxin units which it contains.

The antitoxin is supposed to act in two ways. It neutralizes the toxin that has been formed by the bacilli, and also stimulates the body-cells to the production of further antitoxin. The first property is due to the antitoxic bodies proper and the latter—according to Ehrlich—to altered toxins, called by him toxons. These toxons are not toxic, and, yet, are capable of stimulating antitoxin production in the same manner as the toxin.

We have, as yet, no means of determining accurately the dose of antitoxin suitable to each case of diphtheria. It depends upon the severity of the case, the time of injection, and, to a slight extent, upon the age of the patient. We judge of the severity of the case by the location and extent of the membrane and the degree of constitutional depression. The tendency is constantly toward the use of larger doses of the antitoxin. In the early days of its use the antitoxin was comparatively weak, and large quantities, as much as 20 c.c., were required for a single dose. Many of the unfavorable results at first reported were doubtless due to the large quantities of horse serum which it was necessary to inject. It was also a difficult and painful procedure to introduce such quantities of fluid hypodermically. The antitoxin now used is many times stronger; so that even the largest doses rarely require more than 10 c.c. This concentration of the serum leaves us much more free in increasing the power of the first injection.

Dose.—It is very difficult to formulate rules for the dosage of antitoxin, for the amount required by different cases varies greatly. One patient may require a total of 10,000 units to effect a cure, while another, with a similar type and severity of the disease, will require 40,000.

The slow absorption of the antitoxin from the tissues would seem to make the single injection by far the better method. The tables below show that the single dose gives much greater antitoxin content for the first three days.

(1) ANTITOXIN CONTENT OF BLOOD IN GOATS INJECTED.

(*Each received 5000 units.*)

METHOD OF INJECTION.	Units in 1 c.c. at different intervals of time						
	3 h.	6 h.	12 h.	24 h.	48 h.	72 h.	96 h.
Intravenous	4.0	3.5	3.0	2.6	2.4	2.0	1.8
Subcutaneous...	0.1	0.5	1.0	2.5	2.9	3.0	2.9
Intramuscular ..	0.3	1.3	2.0	2.8	2.8	2.6	2.4

Weight of goats about 25 pounds each.

(2) ANTITOXIN CONTENT OF BLOOD IN THREE ADULT DIPHTHERIA PATIENTS.

(*Each received 10,000 units.*)

METHOD OF INJECTION.	Units in 1 c.c. at different intervals of time.						
	3 h.	6 h.	12 h.	24 h.	48 h.	72 h.	96 h.
Intravenous (1) .	3.0	2.7	2.4	2.0	1.5	1.0	0.8
Subcutaneous (2)	0.1	0.2	0.25	0.4	0.55	0.65	0.7
Intramuscular (3)	0.2	0.35		0.6	0.6	0.59	0.55

Weight of number 1 about 100 pounds; of number 2 about 110 pounds; of number 3 about 120 pounds.

	UNITS IN BLOOD AT			
	12 h.	24 h.	48 h.	72 h.
Single dose............	0.25	0.4	0.55	9.65
Dose divided into three given at 12-hour intervals	0.08	0.2	0.48	0.62

A large series of cases treated by the different methods has also shown that the **intravenous injections of antitoxin** can be safely given. In severe cases of diphtheria intravenous injections are indicated. Park (Jour. of Pharm. and Exper. Therap., March, 1912).

Since antitoxin is practically harmless, it can be given in large doses and repeated as often as the condition of the patient demands. In the nasal and milder forms of pharyngeal diphtheria an initial dose of 4000 to 8000 units in children, and 5000 to 10,000 units in adults, can be given, and the dose repeated in twelve hours if necessary. If there is not marked improvement and the membrane is spreading, there should be no delay in giving repeated doses of 5000 to 10,000 units in children and 8000 to 20,000 units in adults, at six to twenty-four hours' intervals, until there is evidence that the disease is under control. The dose for children will vary with the age and size of the child, but for a child of 2 years the lower doses mentioned will not be too great, and, if necessary, can be exceeded. Usually with a granular appearance of the membrane, with loosening at its edges and relief of the constitutional symptoms in the pharyngeal type, and a relief of the stenosis in the laryngeal, there will be no further use for the serum. The physician should, however, always be ready to give further antitoxin on indication, as it is only with sufficient dosage that cure can be effected.

Intensive use of **antitoxin** is indicated in malignant diphtheria. It is harmless during the three weeks after the first injection, as signs of anaphylaxis do not develop until after this period. In malignant diphtheria the little patient should be watched hour by hour, examining the heart, pulse and urine as well as the throat, and giving antitoxin daily if necessary. Ségard (Annales de méd. et. chir. inf., Sept. 1, 1911).

From all the observations, amounts of **antitoxin** beyond 25,000 units in a child, and 50,000 in an adult, are unnecessary; an initial dose of 10,000 in a child and 20,000 in an adult is probably sufficient for the whole course of the disease. The aim should be to get enough antitoxin into the blood to neutralize any toxin present there, so that no further toxin is able to pass out to the tissue cells. Very few realize that what is given subcutaneously as a single injection is being absorbed for days, and that the accumulation of antitoxin in the blood reaches its highest point from the second to the fifth day. The size of the patient is an important factor in deciding the dose of antitoxin. One should give in the first dose all that is required for the entire disease. Intravenous injection is urged in cases of malignant diphtheria. W. H. Park (Boston Med. and Surg. Jour., Jan. 16, 1913).

Effectual treatment consists in giving a large **initial dose of antitoxin.** In a severe case, from 10,000 to 20,000 units should be injected at the beginning; the result of the first injection will determine whether or no more shall be used. In severe cases of diphtheria 10,000 units by hypodermic injection are advised. If septic manifestations are evident, the most rapid relief follows the injection of 10,000 to 20,000 units into the median basilic vein. Louis Fischer (Med. Record, Feb. 22, 1913).

In the very severe pharyngeal cases, where the physician sees the patient late in the disease, and always in laryngeal cases, an initial dose of 8000 to 15,000 units should be given to a child, and

10,000 to 20,000 units to an adult, this dose to be repeated in six to twelve hours, unless the improvement is very marked. Further treatment is to be carried out according to the reaction of the patient. When there is great improvement in the symptoms the treatment can be tentatively ceased, to be resumed on the least indication. When the improvement is slight, there should be no hesitancy in giving large doses of antitoxin at frequent intervals until there is marked improvement. In severe laryngeal cases it is well to give an initial dose of 15,000 to 20,000 units.

Treatment of 404 cases showing Klebs-Löffler bacilli in smear from culture tubes, admitted from January to November, 1908, showed that provided no complications are present, the best control for the administration of diphtheria **antitoxin** in faucial cases is the patient's temperature. Antitoxin was given by the writers in such dosage, repeated at eight to twelve hours' interval where necessary, that a fall in temperature to the normal line was produced. Practically none of their charts, except those few cases in which complications existed, show a temperature range above normal after the second day. Their average dose of antitoxin was high, but their results were most satisfactory, as evidenced by the comparatively low death rate, early resolution of the membrane, and low percentage of resulting albuminuria.

Gentle swabbing, douching, and gargling of the throat with simple **saline solution,** accompanied by **mild oral antisepsis,** is more efficient and much less distressing than vigorous swabbing and gargling with strong antiseptic solutions, whose tendency is to abrade the mucous membrane, and so produce a fresh raw surface for the spread of the diphtheritic membrane. Mackay and O'Brien (Intercol. Med. Jour. of Austral., Feb. 20, 1909).

Diphtheria should be treated, not only with **antitoxin** injections but also **locally,** and the writer advises the gargling of the throat with a solution of diphtheria antitoxin and physiological salt, 1 to 29, or with a serum diluted with carbolic acid in the strength of 0.5 per cent.; sometimes he has used a spray and, in diphtheria of the nose, swabbing with the solution. Lorey (Med. Klinik, June 30, 1912).

Hot-air inhalations in the treatment of diphtheria. The heated air was conveyed to the mouth by a flexible metallic tube, to the extremity of which could be attached brass tubes of varying diameter, covered by a cork cylinder in order to avoid burning the lips. The highest temperature reached by the air supplied in the apparatus was 150° C. (302° F.), but 110° C. (230° F.) was about the highest point attained in treating the patients. The method followed was either to raise the temperature until there was evidence of discomfort, then at once turn in cold air, and a little later resume the heated air, or more frequently to withdraw the tube from the mouth when the uncomfortable degree of heat was reached, reintroduce it one-half minute later, and so on four or five times, the temperature constantly increasing and the duration of each application decreasing. In adults and adolescents the tongue depressor was used, and the jet of hot air carried directly over the various areas covered with false membrane. The procedure is not painful, is well borne by children, and never produced a burn or other complication. The average number of applications was only four or five, distributed in a period of three or four days. As for the results, the mortality due to diphtheria in the air-treated cases was the same as in those receiving antitoxin, *i.e.,* 15 per cent. The method should be combined with the use of **antitoxin,** since it is complementary, the hot air being chiefly a bactericidal agency, while the serum is chiefly antitoxic. R. Rendu (Lyon méd., Jan. 12, 1913).

The injections of antitoxin may be made upon almost any part of the body, now that the quantity of serum used is comparatively small; the abdomen, thighs, or back may be preferred. An hypodermic syringe capable of holding 5 c.c. is most convenient, but the ordinary hypodermic may be used in emergency. Some slight pain, redness, and edema may be seen at the site of the injection, but nothing more, if proper care be taken in making the injection.

> If the writer had to choose between **antitoxin** and all other measures he would cling to antitoxin. Its injection **intravenously** is the ideal; where this is not practicable he advocates intramuscular injection. The method of injecting the antitoxin at the angle of the jaw, to bring it as close as possible to the primary lesion, has been abandoned as edema is liable to develop afterward, and as intravenous injection accomplishes the same and more. Eckert (Deut. med. Woch., Oct. 24, 1912).

General eruptions may be seen in a large percentage of the cases in which antitoxin is used, if watch be kept for them. The eruption is in the form of an urticaria, as a rule, and develops about the tenth day after the injection. It may be transient and give no trouble, or may continue for several days and be very annoying.

> In cases treated with diphtheria **antitoxin,** the administration of calcium salts for the purpose of preventing or mitigating antitoxin eruptions has been found by actual trial to favor the occurrence and duration of these eruptions. Cassidy (Lancet, Dec. 16, 1911).

> Case of urticarial rash and sciatica following a prophylactic injection of diphtheria **antitoxin.** The patient was a young adult male of good habits, slender build, slightly nervous temperament and somewhat predisposed to rheumatism. Following a prophylactic dose of diphtheria antitoxin (500 units) four years previously he had had a very slight urticaria but no subsequent urticaria up to the present attack, and no previous sciatica. D. Miltimore (Merck's Archives, March, 1913).

Temporary albuminuria has been repeatedly noted after immunizing doses of antitoxin, but this disturbance of the kidneys has always passed off without symptoms or sequelæ.

Swelling of the joints has also been reported in some cases, but must be very rare. These sequelæ of the use of antitoxin seem to be dependent upon the quantity of serum employed in the injection and the number of injections given. These disturbances, the so-called "serum sickness," are more frequent with repeated than with single injections. There seems to be a sensitizing action by the first dose, so that a subsequent one, given within a certain period, is likely to give rise to symptoms. This phenomenon of sensitization has recently been extensively studied and has been termed anaphylaxis.

Park claims that the process elaborated by Gibson for refining antitoxin has reduced the incidence of rashes and "serum sickness" one-half. This process consists of the separation of the antitoxic globulins from the greater part of the non-antitoxic protein, and gives an antitoxin twice to three times as strong as the older methods.

> Authorities up to the present year have failed to emphasize the occasional danger of sudden death in sensitized individuals or those subject to bronchial asthma or to respiratory distress in other forms. Individuals peculiarly susceptible to the odor of horses or stables and those subjects to asthmatic attacks, hay fever, and bronchitis should have horse serum administered only upon most urgent cause, and then with due prophylaxis. Insufficiency or inadequacy of the suprarenal glands may account in the asthmatic type for the peculiar reaction. The administration hypodermically of aqueous extracts of the **suprarenal glands** previous to the use of **serum** in this class of cases is desirable in order to rehabili-

tate and control the vasomotor system, and may prove of great prophylactic value, as well as useful in the heroic treatment of the acute attacks of serum sickness. Wallace (Med. Record, Jan. 7, 1911).

The effects of the antitoxin upon the diphtheritic process may be almost immediate, and should be evident within twenty-four hours in all cases. Although it has no bactericidal power whatever, it affects both the local and the general condition. In the throat an advancing process stops or at once begins its retrogression. The amount of discharge lessens, the swelling diminishes, the membrane ceases to spread, begins to soften, and becomes looser. The favorable influence is quite as marked in the larynx as upon other parts. The stenosis is relieved, as a rule, and the membrane is more rapidly thrown off. The general testimony is that, of the laryngeal cases, a much smaller proportion requires operative treatment for the relief of the stenosis since antitoxin has been used.

If **intubation** is resorted to, the tube is more often coughed out, or can be removed earlier, than under any other form of treatment.

At the Infant Hospital at Moscow during the past ten years the mortality after **intubation** was 52.4 per cent., a figure lower than those reported by a number of other European clinicians, ranging from 76 per cent. (Klein) down to 56.5 per cent. (Thumer). The writer emphasizes the advantage of intubation in diphtheria in early infancy. The chief argument of the opponents of intubation in early infancy is that the larynx is so narrow and small that intubation is very difficult. He met in his ten years' experience in the hospital only three such cases: One was in an infant of 8 weeks, on account of the small size of the larynx, and the other two were in the shape of edema and of spasmodic contraction, respectively. But in all three patients, the intubation was performed. A tracheotomy was found necessary on account of the spasm in only a single instance in which three attempts at intubation has been made. V. I. Moltschanoff Roussky Vratch, Jan. 7, 1906).

In the asphyxia of diphtheria the hypodermatic administration of **morphine** will often obviate the employment of intubation and, even when this operation is essential, that morphine will greatly lessen the length of time that the tube is left in the trachea. Generally the tube may be withdrawn in twelve hours. Of course the morphine is used in connection with **antitoxin.** Lesage and Cléret (Tribune méd., vol. xli, p. 213, 1908).

The constitutional effect of the injection is as marked as the local. Usually the temperature falls within twenty-four hours, the pulse improves, the mind is clearer, and the patient is evidently better in every way.

The cases apparently severe or fatal are transformed into mild ones. Baginsky tells us that, in recording the effects of antitoxin upon the various types of diphtheria, he found it necessary to require his assistants to write their judgment of the severity of the cases upon the admission card, when each case was first seen, since the antitoxin in most cases completely changed the picture.

The time of the injection has a most vital relation both to the immediate effect and to the ultimate outcome of the case. In experimental work an animal can usually be saved from a fatal dose of diphtheria toxin if antitoxin is given within forty-eight hours, but not later. Clinically good results can usually be had if antitoxin is given within three days of the onset of the diphtheria, but later than that its influence is greatly lessened. In the "Antitoxin Report of the American Pediatric Society" the mortality of first-day injections was 4.7 per cent.; of second day, 7.4 per cent.; of third day, 8.8 per cent.; of fourth day, 20.7 per cent., and of fifth day, 35.3 per cent.

Coupling the danger of delay with the harmless nature of the antitoxin, it is quite plain that antitoxin should be given in every case where the diagnosis of diphtheria is probable. Only in mild cases may we wait for the bacteriological diagnosis. Especially in all laryngeal cases should the immediate use of antitoxin be advised.

No harm is done if the case is not diphtheria, and, if it is, a great advantage is gained.

We may safely assume that the use of antitoxin is harmless, for if all the reported cases of sudden death, or aggravation of cardiac or renal disease, or other unfavorable influence were accepted as proved, they could not, for a moment, be weighed against the accumulated evidence of the curative effect of antitoxin in diphtheria.

That evidence has been so fully presented in the articles by Welch, Biggs and Guerard, and the Report of the American Pediatric Society, already referred to, and is so complete, that no attempt is made to introduce it here.

There are certain definite limitations of the efficiency of the diphtheria antitoxin. It has already been pointed out that not all the lesions of diphtheria are produced by the action of the diphtheria bacillus or its toxins.

Certain of them, especially the bronchopneumonia and nephritis, are believed to be due to the action of streptococci.

Upon these processes the antitoxin can have no direct effect. By lessening the depression produced by the diphtheria, antitoxin may enable the patient to resist the further attack of the streptococci or other pathogenic organisms; it cannot be expected to do more. It has also been urged against the antitoxin that diphtheritic paralysis is quite as frequent after its use as it was without antitoxin.

To this two reasonable replies have been made: One, that the nervous system is most susceptible to the action of the diphtheria toxins, and, therefore, most difficult to protect; so that, while antitoxin can save the life of the patient, it cannot protect them from the particular effect of this disease. The other is the ingenious suggestion that, by saving the lives of many who, suffering from severe diphtheritic infection, would, in all probability, have died under any previous form of treatment, antitoxin increases the number of those in whom we should reasonably expect to see diphtheritic paralysis develop.

> The writer having lost 9 children from *diphtheritic paralysis* last year in his 622 cases of diphtheria, while 3 others died of the malignant sore throat without paralysis, he has increased the dosage in such cases and the results have been much better. In 18 unusually severe cases the impending catastrophe was warded off by the repeated large doses of antitoxin, with 5 others in which the ordinary dosage was used, with fatal outcome. His experience confirms the value of this intensive antitoxin treatment in the unusually severe cases, keeping up the antitoxin during convalescence. While it did not prevent the development of paralysis entirely, yet the latter never appeared except in an attenuated form. H. Méry (Archives de méd. des enfants, Sept., 1909).

The method of administration of the antitoxin and its mode of action are such that it in no way interferes with the use of any other form of treatment that may be regarded beneficial. Being given hypodermically, it does not disturb the stomach or interfere with feeding or medication. Fish, of St. Louis, has reported experiments going to prove that antitoxin given by mouth is effective. Similar experiments made by Park gave negative results. It is doubtful whether any advantage would be gained if it were possible to introduce the antitoxin in this way.

> The administration of diphtheria **antitoxin** by mouth is superior to the usual method of giving it by injection. Results are obtained within a few hours and the action of the antitoxin is little slower if any than when it is given by injection. The dose required is also much smaller. The writer has never given more than 4000 units at one time; his usual practice is to give an initial dose of 2000 units and to repeat this dose if necessary. It is often a good plan to give the antitoxin in small repeated doses every two or four hours. There is also less risk of sudden heart-failure that sometimes results from the struggling of children to escape the needle. Cumberlege (Brit. Med. Jour., vol. cviii, p. 2637, 1911).

> The writer recommends diphtheria **antitoxin** by the mouth in every case of infection of whatever nature, but especially streptococcus affections. He gives the following mixture: diphtheria antitoxin, 20 c.c. (⅔ ounce); syrup of lemon or raspberry 30 Gm. (1 ounce); and water 130 Gm. (4⅓ ounces), and has the patient take a tablespoonful of this every hour until bacteriologic examination decides the nature of the infection and the indications for specific serums or vaccines. In five or six years' experience with it he has found it extremely useful and effectual in all forms of infection except actual diphtheria. It is given at the very first symptoms and hence begins to exert its influence before the intoxication has become very intense, while the body needs only slight assistance to rouse the resisting powers. Darier (Presse méd., April 13, 1912).

The reports on the use of **antitoxin** by the mouth lack scientific support. They were based almost entirely on bedside observations. Nedrigailoff (Bolnitchuaja Gazetta Botkina, Jan. 13, 1899) submitted the question to an experimental investigation, and found the administration of antitoxin by mouth or rectum to be without the slightest protective value. His experiments showed that no antitoxin could be found in the blood following its administration by the gastrointestinal tract, and that seven hours after the introduction by the mouth no antitoxin could be found in the stomach or intestines. Recently, Pivovaroff reported before the St. Petersburg Pediatric Society his experiments on guinea-pigs, showing the possibility of immunization against diphtheria toxin by antitoxin administered by the colon. Blumenau and Dzerzhgovsky (Roussky Vratch, March 9, 1913) applied the method clinically with unfavorable results. They then conducted a series of experiments on animals, with the result that in no instance could they secure immunity by this method of introduction of antitoxin; neither could they discover any antitoxin in the blood of the animals so treated. Moreover, even the administration of toxin by the bowel remained without apparent effect. Incidentally, they discovered that the vagina offered a very satisfactory cavity for the absorption of both toxin and antitoxin. In view of the fact that Sokoloff (Pediatria, No. 13, 1912) stated to have employed tuberculin successfully by the colon, the authors administered tuberculin by the bowel to 6 children known to be tuberculous. None of them reacted, although subsequent application of the tuberculin subcutaneous test proved positive. These facts would seem to throw considerable doubt on the efficacy of the method of internal administration of tuberculin recently advocated. So long as the results obtained by various observers at the bedside and in the laboratory are so contradictory, it does not appear to be good therapy to depend on a method so uncertain, particularly in conditions fraught with great danger to the patient. Editorial (New York Med. Jour., May 31, 1913).

Laryngeal stenosis may call for further treatment. The general testimony is that antitoxin exerts a marked, in some cases a marvelous, influence upon diphtheritic stenosis. It is also agreed that since the general use of antitoxin a greater percentage of laryngeal cases have escaped operative interference than ever before, and of those finally operated upon a greater number had recovered. The triumph of antitoxin has been that of **intubation** as well.

Tracheotomy has practically passed out of use in diphtheritic stenosis of the larynx.

Many forms of treatment were formerly combined with the use of antitoxin, but, as the power of the antitoxin has been more fully demonstrated, the tendency to rely upon it has become stronger. At the present time, apart from the general treatment—diet, rest, etc.—after giving antitoxin we confine our efforts to the careful cleansing of the nose and throat and the use of stimulants.

The results of **intubation** after the administration of **antitoxin** have been most brilliant. Whereas two-thirds of such cases died before the use of antitoxin, with it more than two-thirds recover. The indications and technique of the operation are described in the article on INTUBATION.

Tracheotomy should be resorted to only when no trained intubator can be had, or intubation has been tried and has failed. The Continental practice of resorting to a secondary tracheotomy if a tube has been worn four days rests upon no rational basis and should be abandoned. By using hard-rubber tubes, the perfection of which was one of O'Dwyer's last labors, we may leave the tubes in the larynx for months without danger of harm.

The writer advocates small, transverse incisions in **tracheotomy.** The incision should be a transverse cut upon the cricoid cartilage with elevation of a fold of the skin. On bending the head backward the wound opens so that the lower part gapes more than the upper, allowing a good inspection of the topography of this subcricoidal region. In the median line will be seen the linea albicans, which is to be used as a guide to cut through the muscles upon the trachea. This operation avoids severe hemorrhages, and the resulting scar is small and practically invisible. Leede (Münch. med. Woch., June 4, 1912).

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DISINFECTION. See STERILIZATION.

DISLOCATIONS.—DEFINITION.—A dislocation is a permanent, abnormal, total, or partial displacement from each other of the articular portions of the bones entering into the formation of a joint.

A sprain is a temporary, partial displacement, reduced immediately and spontaneously.

In total, or complete, dislocations the articular surfaces are completely separated, or touch each other only at their edges. In ball-and-socket joints the dislocation is said to be complete when the center of the globular head is displaced beyond the rim of the concave socket.

Lesser forms of displacement are termed partial, or incomplete, luxations, or subluxations.

A diastasis is a subluxation in which

the separation occurs in a plane perpendicular to that of the articular surfaces, without lateral gliding of one upon the other. The most frequent examples of this condition are the so-called "subluxation" of the head of the radius in children and the tibiofibular diastasis in Pott's fracture.

A dislocation is complicated by injuries to surrounding tissues of sufficient importance to affect materially the symptoms, prognosis, diagnosis, or treatment. It is rendered compound if the laceration of the soft parts establishes a communication between the cavity of the joint and the outside air.

Symmetrical dislocations on both sides of the body (viz., both shoulders, both hips) are termed double. If they occur in the one bone (jaw, vertebræ), they are called bilateral.

VARIETIES.—Dislocations are classified, according to their etiology, as traumatic and spontaneous. *Traumatic* dislocations are caused not only by external violence, but also by muscular force. Such, for example, as the forward dislocation of the mandible. *Spontaneous* dislocations are due to pathological processes in or about the joint which so weaken its normal supporting structure that luxation occurs gradually (or suddenly) and without recognizable trauma. Occurring in extra-uterine life these dislocations are termed *pathological,* while, if their origin is prenatal, they are *congenital.*

NOMENCLATURE.—Usually the distal member of a joint is said to be dislocated,—the most notable exception is the so-called dislocation of the outer end of the clavicle (acromioclavicular joint), and the direction of the dislocation is that taken by the dislocated bone: thus a backward dislocation of the humerus means that the head of the humerus has been dislocated backward from the glenoid cavity, and lies behind it (unless it has been shifted by a secondary or consecutive displacement). Sometimes, however, we speak of a dislocation as of the joint itself, dislocation of the elbow, of the knee, here, again, the direction of the dislocation being that taken by the distal segment. Thus, instead of saying a "backward dislocation of the humerus," we might say "a backward dislocation of the shoulder." Subvarieties are named, according to the new anatomical position of the distal segment, as subcoracoid dislocation of the humerus, iliac (or dorsal) dislocation of the thigh.

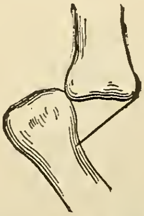
Fig. 1.—Diagram to show the action of a ligament in limiting the range of motion in a dislocation. (*Stimson, "Dislocations."*)

Finally, it is well to bear in mind the distinction between "typical" and "atypical" dislocations, typical dislocations being those in which the attitude of the limb is characteristic, and atypical those in which, owing to the laceration of some opposing structure, whose integrity is usually preserved, the characteristic position is not present. An "atypical" backward dislocation of the hip is the so-called "everted dorsal," in which, owing to the rupture of the outer branch of the Y-ligament, the thigh is everted instead of assuming the usual attitude of inversion and adduction.

SYMPTOMS.—Deformity is always present. The displacement of the articular surface changes the normal contour: a change which can be accurately verified by ascertaining by palpation the abnormal position of the various bony prominences; moreover, the new position of the head of the bone makes a new and abnormal center for the movements of the joint, and, in connection with the restricting influence of untorn ligaments or bony prominences, gives rise to a more or less characteristic attitude and restriction of motion in certain directions.

The comprehension of the causes which produce this constrained attitude and restricted motion, while of great assistance in diagnosis, is, in many cases, absolutely essential to intelligent manipulative treatment, for those same forces that aid our diagnosis we must take into account in our efforts to effect reduction. These forces are purely mechanical. The dislocated bone plays the part of a lever whose long arm extends from the attachment of certain ligaments to its distal extremity, and whose short arm is that part of the bone between this point of attachment and the head of the bone.

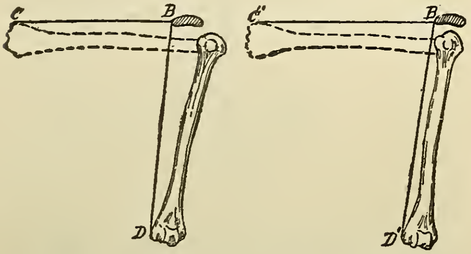

Fig. 2—Diagram to show the effect of attitude upon the measured length of the arm (1) in dislocation of the right shoulder, and (2) when the bones are in a normal position; *B*, *B*, the acromion, ("*American Text-book of Surgery.*")

The figure shows how the ligaments opposite the side toward which the bone has been displaced are put on the stretch by attempts to move the lower part of the limb in the same direction, so long as the head of the bone impinges upon the outer edge of the articular surface or some similar obstacle. Hence the abnormal attitude and restriction of motion in some directions—and possibly abnormal mobility in others, be it noted—and hence, also, the inference that such an obstacle is not to be overcome by brute force, but rather by strategy and dexterity.

Shortening or lessening of a limb is another aspect of the deformity. As a sign, however, it is most unreliable. Fig. 2 indicates the relative positions of the bones in a subcoracoid dislocation of the shoulder as compared with the normal joint. With the arm abducted, the shortening is marked, but in adduction there is little or no shortening; indeed, there may be some lengthening.

Crepitation of a fibrous quality may be elicited during manipulation by friction of the bone over fibrous or cartilaginous structures, and means nothing. True bony crepitus means, of course, a fracture.

Pain is always present, and is due to two causes. There is the primary pain caused by the laceration of the tissues at the moment of the dislocation. This soon passes away. Any persistent pain is due to pressure on nerves or stretching of untorn ligaments, and can only be relieved by the removal of the cause.

Loss of Function.—This is usually complete, and due partly to the pain and partly to the fixation caused by the changed relations of the bones.

Symptoms of Old Unreduced Dislocations.—Deformity of contour and attitude, as well as restriction of motion, will persist as long as the dislocation remains unreduced; but, as the parts tend to adapt themselves to their altered conditions, the disability becomes progressively less, as a general rule, until the functions of the limb can in part be fairly well performed. But several conditions may interfere with this restoration of function. An excessive production of cicatricial tissue may limit or abolish the motions of the joint; the head of the bone may be progressively displaced farther from its normal situation, and the disability thus become greater instead of less, or an intractable neuralgia or edema may result from pressure on adjoining nerves or vessels.

DIAGNOSIS.—The one demonstrative sign of dislocation is the recognized presence of the head of the dislocated bone in an abnormal position. One may make the same inference from the negative evidence; namely, the absence of the head of the bone from its normal situation.

In such localities as the fingers or knee the head of the bone may be seen; elsewhere it may be felt, as in the jaw (forward) or the shoulder, or, again, the diagnosis may only be ascertained by finding an indefinite mass which partakes of the motions imparted to the bone. Measurements may help; but, as above noted, are liable to mislead.

In typical dislocations the attitude of the limb and the limitation of motion are usually the first hint the surgeon obtains of the nature of the case; but, we repeat, the only conclusive evidence is the discovery of the head of the bone out of its normal place.

Differential Diagnosis.—The differentiation of a simple dislocation from a fracture at or near the articular surfaces is often difficult, sometimes impossible. If the fracture is through the neck of the bone (without impaction) the dislocated head will not move with motions imparted to the shaft of the bone; but will, on the contrary, give rise to a bony crepitus, unless some soft parts are interposed. But if the fracture consists simply of the splintering of an articular edge, or the tearing off of a tuberosity, the fragment may be pushed or drawn away and give no evidence, except perhaps a weakness in the joint, a lack of certain motions, or a tendency to recurrence of the dislocation, for which we can only assign the fracture as a probable cause.

The statement that mobility is increased in fracture and decreased in dislocations is misleading and inaccurate. In fractures mobility is not increased, but created where before it was not. In dislocations it is decreased in some directions, but it is not infrequently increased in others, and, indeed, with sufficient laceration of all the soft parts it may be increased in all directions. A dislocation may be readily differentiated from a contusion or sprain by examination under ether.

ETIOLOGY—Predisposing Causes.—Normal predisposing causes exist to a greater or less degree in all joints; they are mainly found in the conformation of the bony surfaces which make up or surround the joint. In some positions there is little resistance to a dislocating force properly applied. Thus, the wide-open jaw may be dislocated forward by a relatively small force, there being but the slightest resistance of bone and ligament to overcome. Or, again, the normal angle at the joint, as at the elbow, predisposes to dislocation by applying a transmitted force (from the hand) in a direction oblique (upward and inward) to the long axis of the joint, and thus tends to force the articular surfaces over each other in an abnormal direction. Moreover, certain outlying prominences may aid dislocation by acting as fulcrums to pry out the head of the bone, as does the olecranon in hyperextension of the elbow and the acromion in hyperextension of the shoulder. Some joints are also more frequently exposed to external violence than others. Pathological predisposing causes are fracture or diseases of the bones, disease of the ligaments or atrophy of muscles that act as ligaments, and distention of the joint with fluid.

Practically all, if not all, dislocations are rendered possible through the primary occurrence of strain of tendons and ligaments, followed by a vulsion of tendons, then sprain-fracture or gross fracture. It is possible, however, that some dislocations are permitted to occur by separation of the fibers of the capsule in place of by sprain-fracture or gross fracture. All dislocations should be skiographed and, if evidence of fracture is not found at first, pictures should be taken in many planes.

All dislocations should be treated as if fracture had occurred, even in the event of negative X-ray evidence. Often there is spontaneous reduction of dislocations, and sprain-fracture or gross fracture is the only evidence left that can be detected by X-ray. The sites of sprain-fractures or gross fractures provide the foci from which the osteoblasts issue, in those cases showing excessive callus or covering of joint surfaces with osseous tissue; moreover, the softer tissues found in joint cavities within a short time after the occurrence of dislocations are often in some stage of transformation into bony tissue. Ross and Stewart (Annals of Surg., Oct., 1912).

Immediate or Determining Causes.—External violence may cause dislocation directly by acting upon the articulation itself, as a dislocation of the humerus by a blow upon the shoulder, or indirectly by force transmitted through the shaft of the bone, as in the same dislocation caused by a fall upon the outstretched hand, or more complexly by leverage, as when a fall upon the shoulder dislocates the inner end of the clavicle upward by leverage exerted on the first rib as a fulcrum.

Muscular action may also be exerted either directly or indirectly. Thus, yawning is a common cause for dislocation of the lower jaw. In fact, some persons can voluntarily dislocate one or other of their joints. The most common example is the backward subluxation of the first phalanx of the thumb; but there are also a few subjects who can throw out their larger joints.

PATHOLOGY OF RECENT DISLOCATIONS.—In joints relaxed by paralysis or effusion (and in the jaw) dislocation habitually takes place without laceration of the capsule. In all other cases (excepting the voluntary dislocations before mentioned) the capsule is torn. In enarthrodial joints the rent is on the side toward which the round head of the distal bone is displaced. In other joints any or all of the ligaments may be torn. The firmer bands, instead of giving way themselves, may strip up the periosteum or tear away the bony prominences to which they are attached. Opposing muscles put upon the stretch may act in the same way. The bones may also be broken by impact on each other; thus fracture of the olecranon occurs in anterior dislocation of the elbow, and a mutual bruising of the head of the humerus and shattering of the rim of the glenoid cavity in dislocations of the shoulder.

COMPLICATIONS.—Fractures worthy of the name of complications may occur. Some, indeed, such as fracture of the anatomical neck of the humerus, may prove insurmountable obstacles to reduction. External wounds, especially if they compound the dislocation, may prove serious complications. Adjoining vessels may be ruptured and give rise to fatal hemorrhage, or to occlusion and gangrene, or to traumatic aneurisms. The rupture of nerves may cause permanent paralysis and anesthesia. The viscera are rarely injured unless by some other associated trauma.

In old unreduced dislocations the lacerated connective tissue about the head of the bone becomes thickened and forms a pseudocapsule, while the periosteum, on which the head of the bone now rests, is stimulated and throws out a ridge of bone so as to form a new articular cavity, sometimes lined with fibrocartilage. The muscles and ligaments shrink or elongate to adapt themselves to their changed circumstances, and thus a comparatively useful new joint may be formed. In the meanwhile an opposite train of events takes place in the old joint cavity. It is obliterated either by adhesion of the capsule or by filling up with granulation tissue. Thus not only is the dislocated bone fixed in its new position, but also the old socket is obliterated and rendered unfit for its reception. It is important to note that the scar may include neighboring vessels or nerves, and by pressing on them give rise to neuralgia or edema without any direct pressure by the bone itself, and, moreover, the tearing of this tissue in attempts at reduction may result in fatal injuries to vessel or nerve.

PROGNOSIS.—Reduction is usually followed by repair of the damage done, and within a few weeks the joint is as useful as ever. Occasionally, however, a permanent laxity of the capsule remains, which allows the dislocation to recur on more or less slight provocation, and with each recurrence the tendency grows more marked. Occasionally, also, without any unusual evidence of injury to the nerves at the time of occurrence of the accident, a dislocation may be the starting point of an intractable neuralgia, or it may predispose the joint to rheumatism. The complications above mentioned render the prognosis more grave.

In old unreduced dislocations the prognosis is different for every individual case. In some the new joint will become fairly useful, in others not so; yet the prospect of relief by operation is none of the brightest.

TREATMENT.—A recent dislocation should be immediately reduced unless great inflammatory reaction, swelling, or shock renders the infliction of pain or the use of anesthetics inadvisable.

Anesthetics are of use to overcome the resistance of the muscles, which, contracted by pain or fear of pain, oppose the manipulations necessary for reduction, or in case the patient can not or will not suffer the pain incident to those manipulations. Reduction may usually be effected in "primary" anesthesia. Ether is safer than chloroform for this purpose.

The choice of the method of reduction depends upon the recognition of the obstacles to reduction. Aside from muscular opposition, the usual obstacle is the resistance offered by untorn ligaments or portions of the capsule to movement in certain directions. Other obstacles are interposition of the ligaments or muscles, and these may be of such a nature as to demand operative interference.

The older methods of reduction by means of direct pressure on the head of the bone or traction by hand, by pulleys, or by electric force have been, in great measure, superseded by the more scientific and practical method of reduction by manipulation, in which, by a succession of gentle movements, the head of the bone is brought opposite the tear in the capsule, the opening is enlarged by relaxation of its sides, and the head of the bone slipped into place by leverage on the untorn portions of the capsule and ligaments, aided, if need be, by traction and pressure on the bone.

In old dislocations the manipulations useful in recent cases are much less likely to succeed, owing to the firm adhesions binding the head of the bone in its new situation and the obliteration of the disused articular cavity. Moreover, strong traction may be required to overcome the contraction of the muscles. Interference in such cases is unavoidably blind and uncertain, and involves much more extensive laceration than took place at the time of the original injury. So many accidents have followed attempted reduction by manipulation in these cases that, if cautious manipulation fails to effect reduction, it is better to leave the dislocation unreduced in the majority of cases, or, if the loss of function is so great as to induce the surgeon to run the risk, an open arthrotomy may be done with the hope of dividing the opposing structures, opening up the old socket, and replacing the dislocated bone.

The accidents which follow ill-advised attempts at reduction are usually fracture of the bone or rupture of vessels, leading to hemorrhage, gangrene, or aneurism. More rarely injury to large nerves has occurred, and even complete avulsion of a limb has been recorded.

After-treatment. — After reduction the joint need usually be kept immobilized only a few days, and excessive motions avoided for a few weeks. Some dislocations require special dressings (*e.g.*, clavicle). Gentle passive motion should usually be begun within at least three weeks to prevent adhesions.

Habitual dislocations have been cured at the inner end of the clavicle by periarticular injections of alcohol (Stimson) and at the shoulder by injections of tincture of iodine. But this method of producing adhesions offers so grave risks of ankylosing the joint that in the more important joints it is advisable, if the tendency cannot be overcome by the prolonged wearing of an immobilizing apparatus, or one which allows only slight motion, to excise, or take a "reef" in, the lax portion of the capsule.

CONGENITAL DISLOCATIONS.—Under this head are included all dislocations supposed to have existed at birth—although sometimes not diagnosticated for months or years—and to have been caused by a maldevelopment of the joint, hydrarthrosis, paralysis, etc. Dislocations produced traumatically *in utero* or during delivery are excluded.

Congenital dislocations of the hip cover about 90 per cent. of all cases. They are more frequent in females than in males. One or both joints may be involved. The typical cases are caused by a defective development of the Y-cartilage and acetabulum, which permits the influence of the weight of the body, or the contraction of the muscles, to drag the head of the bone out of the socket on to the dorsum of the ilium.

Dislocation of the hip-joint which occurs in young infants and children without any apparent violence, usually regarded as congenital, may in reality be due to pressure exerted on the hip-joint during the adoption of the erect attitude of such a nature as to produce displacement of the head of the normal femur from a nearly normal acetabulum. The history of a well-developed girl with dislocation of the hip rarely goes back before the adoption of the erect attitude. The fact that the child is well developed is a considerable factor in the argument in favor of the condition being static rather than congenital. The female hip-joint is weaker and acts at a greater mechanical disadvantage than the male joint. The theory of the dislocation being congenital has so far entirely failed to explain the great preponderance of cases in females. Thompson (Lancet, Sept. 11, 1909).

The term congenital luxation is wrong, as the luxation is not present when the infant is born, but develops later, sixteen, eighteen, twenty, or even twenty-two months after birth, as soon as the child commences to be about. The symptoms are, a cracking noise of the articulation, the difference in the length of the adducting folds, and the exaggerated inward rotation of the femur. When these signs exist one is able to prognosticate the appearance of such a luxation. Gourdon (Presse méd., Sept. 29, 1909).

Dislocation of the hip-joint never occurs in the uterus, but develops after birth. Any malformation in the muscles or in the nerve-centers presiding over them or malformation of the pelvis is liable, however, to induce congenital luxation. Frequently newborn infants display a tendency to dislocation of the hip-joint, but this tendency subsides spontaneously in time in almost every case. Girls are more liable to have it than boys. De Damany and Saiget (Reméde chir., Sept., 1910).

In a study of 17 pelves with double congenital dislocation at the hip-joints, the writer found that the pelvis is tipped very strongly forward, but is not uniformly narrowed except above the brim of the true pelvis. The actual pelvic brim is somewhat enlarged transversely, as is the case with the pelvic cavity below the brim. Occasionally in these cases the whole pelvis suffers from general atrophy. The pubic arch is usually wider than normal. The sacrum is pushed upward and back, and the pressure of the thigh-bone separates the ilia, making the crests straight and the intercrest diameters about 22 cm., and the distance between the spines 22.5 cm. The outlet of the pelvis is larger than normal, especially transversely, and this is true the older the patient, possibly due to the thinning of the pelvic bones. Delmas (L'Obstétrique, Aug., 1911).

Many a congenital luxation of the hip escapes not only the attention of the accoucheur, but many later observers. Obvious symptoms may not appear till the child has reached the age of 4 or 5 years. In one case he describes the child was over 9 years old. Reduction is difficult in such cases and relapse is probable. Roederer (Presse méd., March 30, 1912).

With the uterus pressing on the knees of the fetus little movement is possible for the legs and thighs. Any resistance to downward pulling of the thighs, a rigid uterine wall, small fibroid, legs in extension, feet caught over arms, or forehead, or shoulders, or amniotic folds, extension of the pelvis would develop a force pulling the pelvis away from the femur, that is, a force tending to stretch the capsule and displace the head of the femur upward and backward. Such a force would be a pull transmitted along the length of the femoral shaft, and therefore largely in the direction of the upward displacement. Rixford (Annals of Surg., Dec., 1912).

Pubic and obturator dislocations are very rare. As the child begins to walk the head is pushed farther upward until it is finally arrested and a new joint formed. The head of the bone is small and deformed and the real acetabulum obliterated. Compensatory changes appear in the pelvis, which is tilted forward, and the lumbar spine, which is curved forward. If one hip alone is involved, there is an additional lateral curvature, and the child limps; if both are involved, there is no limp, but the gait is peculiar. The tilting of the pelvis can be made to disappear by placing the child upon its back and flexing the thighs.

The prognosis as to the utility of the limb is fair. The patient will probably be able to get about, and the deformity will grow no worse.

> In establishing the prognosis in congenital dislocation of the hip, the writer classifies the cases under three heads: First, cases in which no serious effort has been made to reduce the dislocation; second, cases which have come to the surgeon too late for a successful bloodless reduction, which the writer reckons as at the sixth year of age in double dislocation and eight years in single dislocation; third, patients who come in time for the bloodless operation to have a prospect of success, *i.e.,* before the above ages. If untreated or ineffectively treated, the prognosis is always bad. At best, there is an unsightly deformity and a defect in gait which are serious enough afflictions, especially for girls. The power of endurance is also impaired and this is likely to be worse with increasing age or to become so after some infectious disease or severe strain. Because traumatic dislocations sometimes recover spontaneously, some still believe that a certain percentage of congenital cases may also do so, but the conditions are different. E. H. Ochsner (Jour. Amer. Med. Assoc., Oct. 22, 1910).

TREATMENT.—Palliative measures should be resorted to in those cases which have reached adult life unrecognized or untreated. For this purpose an elevated sole to the shoe, or a corset stiffened by steel with a pad to limit the upward displacement of the trochanter may be used.

Reduction by forcible manipulation, as perfected by Lorenz, is especially applicable in children from 2 to 7 years of age. Under anesthesia the leg is forcibly rotated outward and inward, then abducted so that the thigh lies at right angles to the trunk in the flexed position. During this process the adductor muscles are forcibly massaged. Forcible flexion until the thigh touches the abdomen is carried out. The child is then placed on its face and the leg hyperextended and abducted. The force of these manipulatory movements must be sufficient to relax the muscles completely. The reduction is accomplished by abduction, rotation, and flexion, as in the traumatic cases, and in favorable cases the head slips into the acetabular cavity with a click. After reduction a plaster spica bandage is applied with the limb in a position of right-angled flexion and abduction. After two weeks the cast may be cut away below the knee and the child allowed to walk. This bandage is removed in two or three months and the leg put in a less degree of flexion and abduction for three months longer. Fixation should be continued until the joint stability is assured, and usually consumes a period of from six months to a year. After the removal of the cast massage, active and passive movements, should be thoroughly carried out.

> In his experience with 800 cases of bloodless reduction of congenital dislocation of the hip-joint, the writer found that bloodless methods always gave better results, his later series showing from 85 to 90 per cent. of perfect function for unilateral dislocation and 30 per cent. for the bilateral. He applies treatment as soon as the dislocation is recognized and when the child can keep itself clean. After the age of 7 the results are uncertain and 10 is the extreme limit for bloodless measures. Redard (Annales de méd. et chir. infantiles, July 15, 1910).
>
> The difficulty of keeping the children clean is the great drawback to applying orthopedic appliances to very young

children, but this is far outbalanced by the superiority of the results when treatment is begun early, when the child is from 1 to 3 years old. The children wearing the appliance should use a special flat bedpan; those that cannot be trained to use this vessel should sleep in little hammocks with large meshes through which the excreta fall into a vessel below. Le Damany (Arch. gén. de chir., March 25, 1912).

For older cases or cases in which the above does not succeed, the open operation is indicated.

Early diagnosis and prompt treatment are essential. Left untreated, further deformity results, limping and scoliosis with unilateral dislocation and lordosis when the deformity is bilateral. The bloodless method gave him functional recovery or great improvement in over 90 per cent. of his cases, the few failures being due to neglect of the limits imposed by age or to lack of proper co-operation on the part of the family. No child is too young for treatment, but bilateral dislocation can seldom be successfully corrected after the age of 6 and unilateral after 10. The most auspicious age is during infancy. O. Vulpius (Med. Klinik, Nov. 28, 1909).

The writer successfully corrected a congenital dislocation of both hip-joints in a woman of 26. He scooped out a new cavity for the head, but broke off the head in fitting it into the new cavity. The neck stump answered every purpose, however, and the functional use of the limb was restored. A similar operation was then done on the other hip-joint six months after the first and without a fracture this time, so the patient was restored to practically normal gait. Patschke (Deut. med. Woch., Sept. 14, 1911).

Of the operations, that of Lorenz is a type. He makes a vertical anteroexternal skin incision, divides the fascia lata transversely, separates the muscles, frees the bone by a cross-cut in the anterior surface of the capsule, gouges out the old acetabulum, making a strong upper rim to it, and replaces the bone by extension, aided by a traction apparatus. Immobilization is replaced by passive motion at the end of four weeks, and the child begins to walk with assistance two weeks later. No further apparatus is used. In difficult cases Lorenz advises a preliminary course of two weeks' extension by a thirty-pound weight.

The bloodless method (Lorenz) consists in movements in forced flexion, extension, abduction, and adduction to stretch the muscles. When these are sufficiently stretched the head is brought into the acetabulum. The leg is held in a position of abduction and extension at right angles to the body by a plaster spica to the knee and kept so for nine months with gradual reduction in the amount of abduction and extension. The method is only applicable to young children before the seventh year.

The operation of choice is the Lorenz operation, and here, when the patients have passed the age limit, the results are not very promising, though a reduction of dislocation can usually be temporarily obtained. The open method of reduction is not justifiable in double dislocations, though the case is different in single ones. The writer has had two patients with double dislocations, in each of whom he was able to reduce one hip by the bloodless method, and, failing to reduce the second hip, he subsequently employed the open method and obtained fair results. He has treated 26 patients below the age limit, 17 of these with single dislocations, and reduction was secured in all with good success. Nine patients, or 18 hips, with double dislocations below the age of 6 were treated. Reduction was secured in 14 hips by the bloodless method and 10 of these have been out of the cast for a year or more; 9 of the 10 had good anatomical functional result, 1 relapsed after the cast was removed. Good anatomical functional results were obtained altogether in 10, or 71 per cent. The 4 still in casts were in good condition when last seen. The two assertions that he can make without fear of contradiction are that, first, no patient should go undiagnosed beyond the age of 3, and, second, if properly treated at this age the majority can be successfully reduced and good functional and anatomical results obtained. He cautions against the use of too great force, especially suddenly. Another common error is to reduce by bringing the head of the bone around the lower border of the acetabulum instead of over the posterior rim. He thinks that this is one of the principal causes of the large number of anterior transpositions and also for the large number of failures in the hands of some operators. When reduction is once accomplished the hip should never be intentionally reluxated. The hamstring tendon should not be stretched at the time of reduction. Their action is fully as important in holding the head opposite the Y-cartilage as is the subsequent weight bearing. The tenseness of the hamstring muscles is a very valuable sign for the first couple of weeks that the hip has not reluxated. The cast should be applied over stockinette instead of glazed cotton. If the bony prominences are protected by a little felt or quilted gauze, this will be much more comfortable than cotton padding, and it holds the head a great deal more firmly. The cast should be applied with the thighs abducted to a right angle and flexed to a right angle, and should be left in place for a year from the time of reduction with only one change of cast. The writer believes that development of the cotyloid cartilage is a most important factor in the permanency of the reduction. Ochsner (Jour. Amer. Med. Assoc., Oct. 22, 1910).

Early treatment of congenital dislocation of the hip is always indicated; otherwise, like most congenital and many acquired deformities, it tends progressively to become more disabling as the patient grows older, while, within certain limits, the earlier it is taken in hand the easier is the treatment and the better are the results. The writer considers Lorenz's method as the most satisfactory. W. C. Stevenson (Dublin Jour. of Med. Sci., June, 1912).

The anterior knee dislocations are easily reduced, and a good functional result may be predicted.

PATHOLOGICAL DISLOCATIONS.—Paralytic ("myopathic") dislocations occur usually in the shoulder, where the deltoid and scapular muscles form such important accessories to the joint.

Dislocations by effusion, erosion, or other articular processes occur in the course of the eruptive, continued, or rheumatic fevers. The hip is commonly affected.

SPECIAL DISLOCATIONS.

Dislocations of the Lower Jaw.—The dislocations may be single or double. Upward or backward dislocations are very rare. In the former the condyle is driven through the base of the skull; in the latter, back through the anterior wall of the external auditory meatus.

Forward Dislocations.—The lower jaw projects forward, the mouth cannot be closed, the condyles may be seen and felt in front of the eminentia articularis. The glenoid fossa is empty. In unilateral dislocations the chin is deviated to the opposite side. The pain is usually not great.

The usual cause of forward dislocations is a wide opening of the mouth in yawning, laughing, or introducing some large object. It is more frequent in women than in men. When the mouth is wide open the external lateral ligament is relaxed and the external pterygoid muscle draws the condyle, and the interarticular cartilage with it, well forward on the eminentia articularis. A slight overaction of this muscle carries the condyle over the summit, and is then held by the balance of forces between the muscles pulling upward and forward and the external lateral ligament pulling upward and backward. The interarticular cartilage accompanies the condyle, at least part of the way. The capsule is not torn.

Reduction is accomplished by opening the mouth more widely to relax the ligament and then pressing the condyle backward and then a little downward. A fairly successful method is by grasping the jaw on either side with the thumbs on the molar teeth and the fingers under the jaw outside. As the jaw snaps back the thumbs must be quickly slipped into the hollow of the cheeks to avoid being bitten. Reduction of one side at a time is sometimes easier. Anesthesia may be required to overcome the contraction of the muscles.

Not infrequently this dislocation tends to become habitual. To overcome this the meniscus may be sutured in place. Injection of tincture of iodine has been proposed.

> Dislocation of the entire upper jaw caused by a horseback accident, the upper jaw being separated from the base of the skull. The writer restored it in place by means of an appliance exerting pressure by a band passing around an upright rod at the back of the neck, worn for three weeks, and followed by a dental appliance. By the end of six weeks articulation was apparently normal. Thölet (Deut. Zeit. d. Chir., Sept., 1909).

Dislocations of the Spine.—Dislocation of the lumbar and dorsal vertebræ is almost always complicated by and confounded with fracture. Extension and local pressure have occasionally effected reduction; operative treatment should be resorted to in hopeful cases.

Dislocations of the occiput (from the atlas) and the atlas (from the axis) have been diagnosed *post mortem.* Laceration of the medulla, with or without fracture of the odontoid process, causes instant death in most cases.

> Case of fracture and dislocation of the atlas with recovery. The patient was placed on his back and a collar around the chin and occiput applied, from which an eight-pound weight, over a pulley, was suspended. The head of the bed was raised about four inches, to overcome the traction. The pain at once became less severe; the paralysis after several weeks began to recede, first improving in the feet, then the legs, then the body, later the arms, and last of all the forearms. After allowing the patient to get out of bed an ambulatory extension apparatus was applied and worn for several months. At the present writing after nearly two years since the injury, the hands present evidence of paralysis. The fingers are clumsy, the interossei are atrophied, and the strength of the hands is very much impaired. The neck is much less rigid; there is no pain on attempts at motion. Swallowing food, at first difficult, is now easy. The patient at the present time is doing some manual labor, and is in good general health. Carson (Annals of Surg., Nov., 1911).

Dislocation of the Lower Cervical Vertebræ.—This may be double or single, complete or incomplete, forward or backward, or bilateral in opposite directions. If the dislocation is unilateral (forward), the head is turned to the opposite side, on which side the muscles are contracted. On the side of the dislocation the dislocated bone may be felt, and its spinous process is deflected toward that side. In bilateral forward dislocations the head may be bent far forward and the dislocated bone (usually the fifth) felt in the back of the neck, or the head may be extended and the bone palpable within the pharynx.

The symptoms depend upon the amount of injury to the cord. Damage to the cord above the third cervical vertebra causes death by cutting off the phrenic nerves. Below this point the result will be a paralysis more or less durable according to the nature of the lesion.

The mechanism of the unilateral forward and bilateral dislocations in opposite directions is abduction (lateral flexion) and rotation, by which the inferior articular process of the upper vertebra is lifted over the superior process of the lower one. Bilateral forward dislocations are caused by hyperflexion; backward, by hyperextension and direct pressure.

In every compression fracture of the bodies of the vertebræ with injury of the spinal cord, as shown by the X-rays, operation should be done. The object of the operation should be to lay bare part of the cord at which pressure occurs by removing the arches of the vertebræ. It is necessary to section the pair of nerves just above or below the dislocated vertebra in order to prevent the bending of the cord by their traction upon it. Provision must be made for hemostasis not only to render the operation easier, but to prevent too great loss of blood, which is apt to occur in this region because of the rich vascular supply. This can be done in connection with the soft parts by means of provisional ligatures placed lengthwise parallel to the proposed line of incision and in the dura and bone by means of adrenalin solution. The loss of spinal fluid during the operation is lessened by the inclined position. Loss of spinal fluid on the day following the operation is of no significance. The disadvantages arising from its loss can be compensated for by subcutaneous injection of salt solution.

In order to prevent undue mobility of the spine after operation a plaster cast should be put on while the patient is still on the operating table. Robertson (Deut. Zeit. f. Chir., Bd. civ, H. 1-2, 1910).

Treatment.—Reduction should be attempted at once. Unilateral dislocations are to be reduced in the way they were produced, *i.e.*, by increased abduction and traction (to free the edge of the process), followed by adduction and rotation, aided by direct manipulation, so as to lift the disarticulated bone back into place.

Traction and local pressure have proved effectual in the reduction of bilateral dislocations.

After the reduction the patient should be kept quiet for some weeks. A plaster-of-Paris splint for head and neck is advisable.

These means failing, if there seems any hope of recovery by removing the pressure from the cord, the dislocation should be cut down upon aseptically and an attempt made to reduce it by removing such ligamentous or bony obstacles as may exist.

Dislocations of the Sternum.—Dislocations, forward or backward, of the body from the manubrium are usually accompanied by serious interference with respiration and circulation. From fracture the diagnosis is made by finding the second costal cartilages attached to the manubrium and torn from their articulation with the body. Inasmuch as the injury is due to great violence, direct or indirect, the associated injuries play a large part in the prognosis. Reduction is effected by dorsal flexion and direct pressure.

Dislocations of the ensiform process are a tilting either forward or backward. The symptoms are pain and persistent vomiting. Pressure with the fingers or with a sharp hook introduced underneath the skin will reduce the dislocation.

Dislocations of the Ribs and Costal Cartilages.—The ribs may be dislocated forward from the spine or forward or backward from each other or from their costal cartilages. The cartilages may be dislocated from the sternum.

The symptoms and treatment are the same as of fracture of the ribs. Reduction, followed by the application of a tight band of adhesive plaster three-fourths of the distance around the chest. Chondrosternal dislocations usually recur.

Dislocations of the Inner End of the Clavicle.—The clavicle may be dislocated forward, backward, or upward, in this order of frequency.

Forward dislocation may be complete or incomplete. The head of the bone is prominent and may be displaced inward. The shoulder sinks downward and inward. The arm is useless. There is local pain. This dislocation is usually caused by a forcible depression and pushing backward of the shoulder, by which the center of the clavicle comes to rest on the first rib, and on it as a fulcrum the inner end is pried upward and forward. By pulling the shoulder upward and backward and pressing on the dislocated bone reduction is effected; but retention is often difficult. Dorsal decubitus with the shoulder pressed forward may prove effective or may be reinforced by direct pressure by a molded plaster-of-Paris splint, a hernial truss, or a pad retained in position by adhesive plaster, or a figure-of-8 bandage, crossing in front. If all precautions fail and the dislocation becomes habitual, two or three biweekly injections of alcohol with immobilization may be attempted, or the capsule exposed and shortened.

Backward dislocations may be either complete or incomplete. The head of the bone passes backward and may compress any of the important structures at the root of the neck. This dislocation may be caused by direct violence or by forcing the shoulder forward and inward. Reduction is effected and maintained by drawing the shoulder backward and outward and retaining it in that position.

Upward dislocation is caused by depression of the shoulder. The head of the bone rests on the episternal notch, having passed behind the sternal head of the sternomastoid. Reduction is made by drawing the shoulder upward and outward and pressing the head of the bone down. Here, again, retention is difficult, and Malgaigne's patellar hooks have been suggested as an adjunct to the treatment.

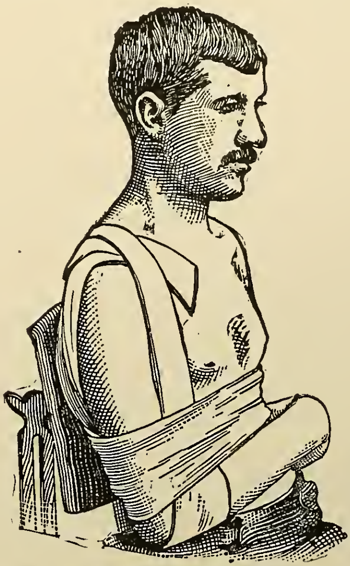

Fig. 3.—Adhesive-plaster dressing for upward dislocation of acromial end of clavicle. ("*American Text-book of Surgery.*")

Dislocations of the Outer End of the Clavicle.—The usual variety is upward or upward and outward. Rarely a subacromial dislocation occurs. The so-called subcoracoid dislocations are probably mythical.

Upward Dislocation.—The acromial end of the clavicle rises more or less above the acromion, and may be displaced outward over it. There is frequently fracture of the articular edges. The usual cause is a blow on the shoulder. Reduction is easy; retention, difficult. Non-reduction causes almost no loss of function and but little deformity. Stimson's retention dressing is recommended for its simplicity and efficiency (Fig. 3). A long strip of adhesive plaster three inches in width is placed with its center under the point of the flexed elbow and its ends carried up in front of and behind the arm, crossing over the end of the clavicle, and secured to the front and back of the chest, respectively, while the bone is held in place by pressure upon the clavicle and elbow.

Recurrence can be readily detected through the plaster. For additional security the forearm should be supported in a sling, and the arm bound to the chest.

Subacromial Dislocations.—A few cases are recorded in which the outer end of the clavicle was forced down and caught under the acromion. Direct violence and muscular action are the recorded causes. Reduction was easy by drawing the shoulder outward, and there was tendency to recurrence in only one case.

Dislocations of the Shoulder.—These dislocations are as numerous as all other dislocations taken together. They are rare in youth and old age, and more frequent in men than in women. This frequency is explicable by the exposure of the joint to trauma and its conformation. The glenoid cavity covers such a small part of the head of the humerus that, in extreme degrees of abduction, extension, or flexion, any force transmitted through the shaft of the bone is applied obliquely in the bony surface and directly on the capsule of the joint, through which the head of the bone is then forced.

Varieties.—Four divisions may be made according to the direction in which the head of the bone leaves the socket, and these subdivided according to the point at which it comes to rest, or according to the position of the limb, as follows:—

Anterior ...	Subcoracoid (most common). Intracoracoid (exceptional). Subclavicular.
Downward..	Subglenoid (uncommon). Erecta (very rare). Subtricipital.
Posterior ...	Subacromial (rare). Subspinous (very rare).
Upward	Supraglenoid (very rare).

In the anterior dislocations the displacement is also more or less downward (and, of course, inward), and in the downward ones it is usually also forward and inward. Thus, the two classes merge into each other. The term "subglenoid" is restricted to those cases in which the head of the bone is very low, others of this class being called "subcoracoid." The accompanying figure (Fig. 4) will demonstrate the different positions assumed by the head of the bone in the anterior-and-downward dislocation.

Anterior Dislocations.—The subdivisions of this variety are dependent on the increasing amount of inward displacement of the head of the bone, and grow less frequent in the same order; namely, subcoracoid, intracoracoid, and subclavicular.

Subcoracoid.—The head of the humerus lies beneath the coracoid process, in contact with it or at a variable distance—a finger's breadth at most—below it. The head may be displaced inward until three-fourths of its diameter lies to the inner side of the process (farther inward would be intracoracoid) or it may be simply balanced on the anterior edge of the glenoid fossa. The elbow hangs away from the side and the deltoid fullness of the shoulder is lost (Fig. 5). The axis of the humerus is seen to pass to the inner side of the glenoid fossa, and palpation reveals the absence of the usual bony resistance below the outer side of the acromion, and the presence of an abnormal resistance below the coracoid process, or in the axilla, which partakes of rotary movements communicated to the arm. Voluntary movement is usually lost. Passively the arm can be abducted, but not so adducted that the elbow can touch the chest and the fingers rest on the opposite shoulder. Measurement in abduction shows shortening.

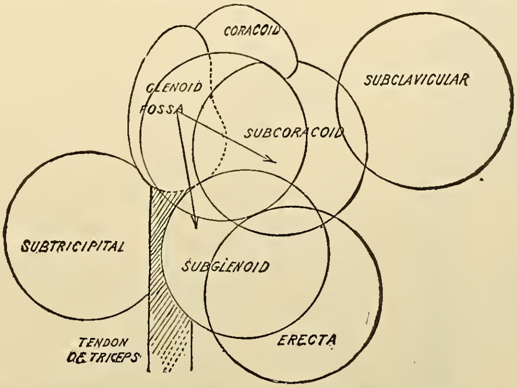

Fig. 4.—To show the range of positions that may be taken by the head of the humerus after primary displacement forward or downward in any of the directions between the arrows. (*Stimson, "Dislocations."*)

The diagnosis is usually easily made by finding the glenoid cavity empty, the head of the bone beneath the coracoid, and by eliciting the above-mentioned sign. If there be fracture of the anatomical neck the head, if it can be felt, will not participate in movements imparted to the shaft, and crepitus can usually be elicited.

The writer calls attention to the pathognomonic contracture of the joint—extreme inward rotation—which may occur with sprains, dislocation or even with effusion or slight inflammation in the shoulder; the joint is abducted and pivoted forward by 30 or 40 degrees. This position is not due to the action of the peripheral part of the joint, the upper arm, but to torsion of the central part, the scapula. The swelling, atrophy of the deltoid and tenderness of the joint are important for differentiation. If only the region of the subacromial bursa is tender, the joint itself is probably not injured; tenderness of the entire anterior capsule speaks for dislocation. To bring the scapula into place, the patient should raise and abduct the arm until the scapula stands even with its mate. Then an assistant should hold the shoulder girdle firm while the passive movability is tested; if it proves difficult to lift the arm backward and twist it outward, the diagnosis of dislocation is certain. Treatment should aim to rest the joint and promote absorption of blood or effusion for a few days, and then efforts should be made to exercise the anterior capsule to ward off atrophy. He gives illustrations of the simple exercises which he has found best adapted for this; they are done for five minutes several times a day. The seated patient is fastened to the chair with a band passed over the shoulder and the lower rung of the chair, while a second band below the axillæ fastens the trunk to the back of the chair. The arm is drawn backward by a loop passing around the arm above the elbow, with which a weight is drawn up over a pulley some distance to the rear, on a level with the top of the patient's head. This combats the tendency to inward rotation. Another exercise is with the pulley on a level with the elbow and the loop passed over the wrist, the arm tied back above the elbow to the back of the chair. F. Lange (Jour. Amer. Med. Assoc.; from Münch. med. Woch., June 4, 1912).

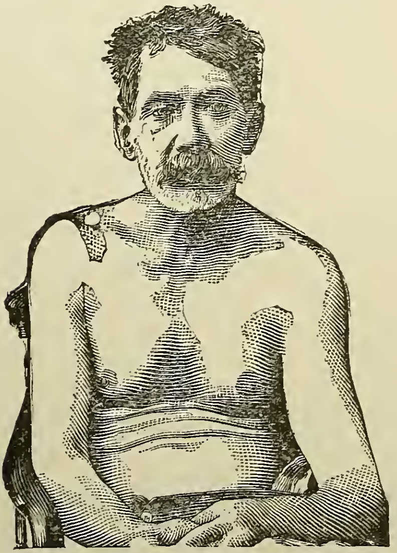

Fig. 5.—Subcoracoid dislocation of the left shoulder. (*Stimson, "Dislocations."*)

Causes.—Direct violence, by a blow upon the shoulder; indirect, as by a fall upon the hand; by leverage in forcible abduction and outward rotation; or by muscular action in any of the above ways.

Pathology.—The capsule is torn at its inner and lower portion, or, more rarely, stripped up, and with it may be torn the circumflex nerve, the posterior circumflex artery, and subscapularis (Fig. 6). In "typical" cases the outer and upper portions of the capsule remain untorn and aid in determining the abduction. The supraspinatus, infraspinatus, and teres minor may be torn away (in decreasing order of frequency) from the greater tuberosity, or there may be avulsion of more or less of the tuberosity itself. With avulsion of the tuberosity the tendon of the long head of the biceps may slip to the outer side of the bone and oppose reduction (rarely). This tendon may also be torn. The head of the humerus may be bruised and ground by impact upon the edge of the glenoid cavity, which, in turn, is splintered.

Treatment.—In uncomplicated cases reduction is usually easy by Kocher's method, as follows:—

The elbow is flexed to a right angle and pressed closely to the side; then the forearm is turned as far as possible away from the trunk,—external rotation of the arm (Fig. 7). Maintaining the external rotation, the elbow is carried well forward and upward,—flexion of the arm (Fig. 8), and, finally, the hand swept over until it touches the chest,—inward rotation (Fig. 9),—the elbow being simultaneously lowered. Anesthetics may or may not be necessary. If, after the "first movement," the head does not roll out in front of and below the acromion, the attempt will fail. Direct manipulation of the head may be of assistance.

If Kocher's method fails, traction downward and outward (never upward and outward, on account of the danger of lacerating the vessels) should be tried. After a long, steady pull, manual or elastic, the muscles may yield and allow the head of the bone to be pushed back into place. Or, after a few moments of traction, the arm is forcibly adducted over the closed fist in the axilla (this is safer than the heel). If anesthetics are used, all of these forcible measures should be executed very cautiously.

> The writer has for the last twenty years successfully reduced all his cases of shoulder luxation by the use of a modification of Kocher's well-known method. The latter procedure is carried out in four steps: 1. Flex the forearm to a right angle, with the elbow pressed against the side of the body. 2. Carry the hand outward, causing external rotation of the humeral head. 3. Maintaining the hand in this position, move the elbow forward, inward and upward. 4. Carry the hand rapidly toward the sound shoulder. The author dispenses entirely with the fourth step, stating that if proper gentleness and deliberation be used, the head of the humerus returns to its normal position in the glenoid cavity while the third movement is being performed. This movement should be carried out slowly, and brought to a stop at the point when maximal resistance is offered. After a moment's delay a slight jolt is felt, which signifies that the head of the humerus has reentered the glenoid fossa. An essential part of the procedure consists in manipulating gently, in order to avoid causing pain and consequent firm contraction of the muscles governing the joint. The patient should preferably be kept ignorant of the fact that reduction is about to be performed, voluntary resistance being thereby eliminated. M. G. Gallois (Bull. méd., Dec. 11, 1909).

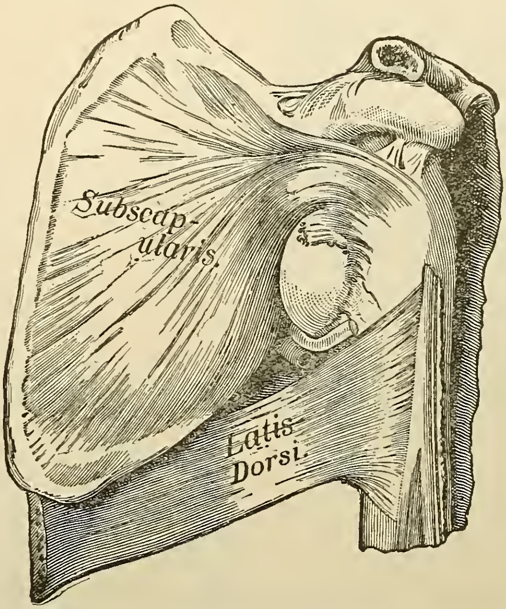

Fig. 6.—Subcoracoid dislocation on a cadaver, showing rupture of lower part of subscapularis. (*B. Anger, in Stimson's "Dislocations."*)

Prolonged traction upon the abducted arm by India rubber or a weight and pulley, or with the body horizontal and the arm dependent (Stimson), as in Fig. 10, will usually reduce easily in a few minutes.

If judicious attempts at reduction by these methods fail, even under anesthesia, an open arthrotomy should be done for the purpose of discovering and removing the obstacle to reduction.

In intracoracoid dislocations the head is displaced farther inward and the symptoms are those of the subcoracoid, except that the head of the humerus is felt farther displaced and the shoulder is more flattened. The arm may be fixed in horizontal abduction. The cause of this particular dislocation is, as a rule, an unusual amount of laceration of the capsule and subscapularis, which allows the head of the bone to pass farther inward. Reduction by outward traction is easy unless the subscapularis or a torn portion of the capsule intervene. In such cases operation is the only recourse.

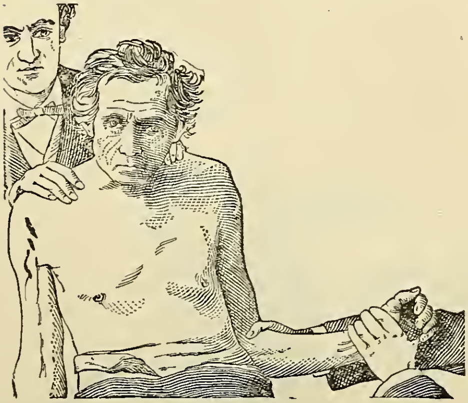

Fig. 7.—Kocher's method of reduction by manipulation. First movement, outward rotation. (*Ceppi, "American Text-book of Surgery."*)

The writer has used successfully during forty years the following simple method of reducing dislocation of the shoulder. The forearm is held between the physician's thighs as he stands in front of the seated patient. The arm is held firm by the adductor muscles and strong pressure can thus be brought to bear as the physician pulls back while holding the shoulder with his hands. The downward pressure thus exerted overcomes the action of the antagonist muscles and stretches the capsule and ligaments until reduction is easily done. The only assistance required is some one to hold the patient firm in the chair, one arm around his neck and the other in the axilla. This technique allows rapid reduction of even old dislocations without anesthesia, assistance or apparatus. Schichhold (Med. Klinik. April 16, 1909).

Nothing is worse for a shoulder luxation than immobilization in the usual sling, and the writer advises immediate massage and movement of the joint, which should never be delayed beyond twenty-four hours. This treatment will do away entirely with the poor results formerly so common. Yvert (Presse méd., June 17, 1911).

The writer seizes with his right hand the hand of the dislocated member, which is thrown about the operator's neck, and with the free left hand directs without difficulty the head of the humerus, extending, counterextending, and reducing at will. The operator is thus able to apply extension, counterextension or reduction and needs no assistant. Angelvin (Semaine méd., March 20, 1912).

In subclavicular dislocations the same forces acting more energetically force the head of the bone still farther inward.

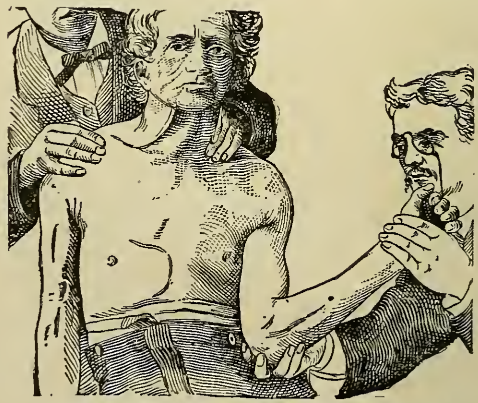

Fig. 8.—Kocher's method of reduction. Second movement, elevation of elbow. (*Ceppi, "American Text-book of Surgery."*)

Downward dislocations include all cases in which the head of the bone lies below the glenoid fossa. In subtricipital dislocation, of which one case is recorded, the head of the humerus was displaced secondarily backward and upward behind the long head of the triceps.

Subglenoid Dislocations.—The symptoms are those of subcoracoid dislocation; but abduction and flattening of the shoulder more marked. The head of the bone is palpable below its socket. The upper part of the greater tuberosity is habitually torn away. The usual cause is forcible abduction followed by rotation or impulsion.

The treatment indicated here is traction in moderate abduction with direct pressure.

Luxatio Erecta.—Very rarely, by forcible elevation of the arm, the head of the bone is displaced so far downward that the extremity maintains its erect position. It is reduced by upward traction until the head falls into place.

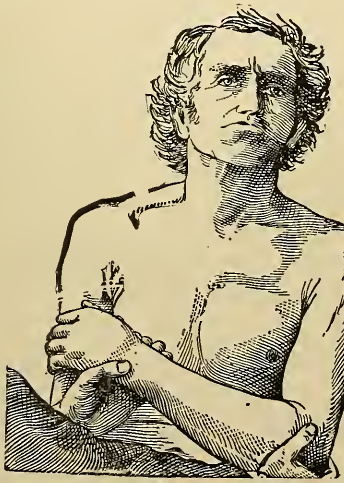

Fig. 9.—Kocher's method of reduction. Third movement, inward rotation and lowering of elbow (*Ceppi, "American Text-book of Surgery."*)

Posterior Dislocations.—The two varieties differ only in the extent of displacement.

Symptoms.—The arm is adducted and rotated in, the elbow being directed slightly forward. The shoulder is flat in front and full behind (where the head of the bone may be felt). Passive motion is restricted; voluntary motions absent.

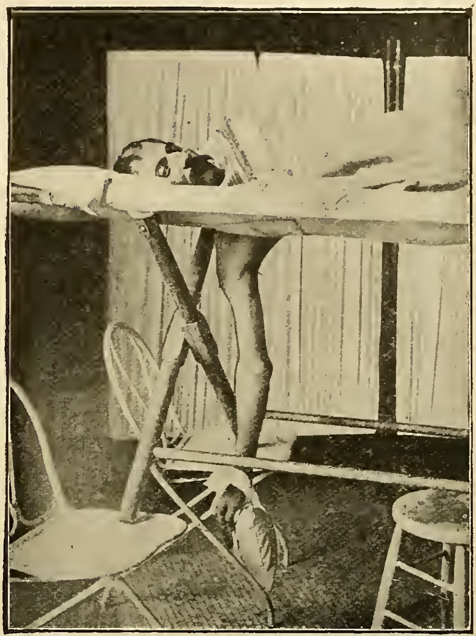

Fig. 10.—Reduction of anterior dislocation of the shoulder. (*Stimson.*)

The cause is direct pressure outward and backward, or the pressure exerted in the same direction along the adducted and inward-rotated humerus.

The outer side of the capsule is torn and the external and internal scapular muscles more or less lacerated or avulsed with fragments of the tuberosities. The head of the bone lies on the outer edge of the glenoid fossa, or farther back beneath the spine of the scapula, or on the infraspinatus.

Treatment.—Reduction is accomplished by traction and direct pressure forward. Avulsion of the subscapularis makes recurrence probable. Unreduced dislocations backward are accompanied by an unusual amount of disability.

Upward Dislocations.—These are extremely rare. The head of the bone is forced upward between the coracoid and acromion, usually to above the clavicle. The arm is almost immobilized in adduction and slight extension. Reduction may be effected by downward traction.

Complications of Dislocations of the Shoulder.—Compound dislocations are very rare, and are commonly caused by direct violence. The skin wound is usually in the axilla. Aside from complications which may exist not dependent on the dislocation, the great dangers are from laceration of the main arteries (frequent) or nerves (unusual) and from suppuration. The treatment consists of enlarging the wound until the extent of damage can be fully appreciated and, as far as possible, repaired. Meanwhile the wound should be thoroughly irrigated with "normal" salt solution. The dislocation may now be easily reduced. In most cases thorough drainage should be provided for, and in some cases it may be advisable to excise the head of the humerus to this end to oppose ankylosis.

Fractures of the various bony prominences of the scapula and humerus have commonly a purely pathological importance. Fractures of the anatomical or surgical neck of the humerus are important, but often difficult to diagnose. The diagnostic points of fracture of the anatomical neck are the recognition of the head in the axilla and its failure to move with the shaft, the maintenance of nearly normal range of motion, and the normal position of the greater tuberosity. Crepitus may sometimes be elicited. In fracture of the surgical neck the signs are quite the same, except that the tuberosity is displaced with the head, and, with it, fails to move with the shaft, and crepitus is more easily elicited. In either case the upper fragment may be reducible by direct manipulation. This failing, if the fragments can be approximated, the arm may be immobilized for three or four weeks in an appropriate position with the hope of obtaining union and effecting reduction at the end of that time by manipulation. But the better plan is probably to do an open arthrotomy and remove the upper fragment, except in such fractures of the surgical neck as can be reduced, and to this end the use of a strong right-angled hook inserted into a hole drilled at the lower end of the upper fragment may be of great service (McBurney). Or a fairly useful false joint may sometimes be obtained at the point of fracture.

Injuries to Vessels and Nerves.—The axillary itself is very rarely ruptured, and, hence, the radial pulse may persist, even though there be serious damage to the smaller arteries about the joint. This damage is usually due to ill-advised attempts at reduction, and is recognized by the rapid extravasation of blood down the arm and into the axilla. Treatment is by pressure, ligature of the axillary at the rupture or of the subclavian, or disarticulation at the shoulder. The mortality is very high. The circumflex nerve is sometimes torn, with a resulting temporary or permanent disability of the deltoid and anesthesia of the shoulder.

Treatment of Old Unreduced Dislocations.—If the dislocation cannot be reduced after loosening adhesions by forcible (yet judicious) rotation and traction, operation is advisable for reduction by division of the soft parts, or for excision of the head of the bone. A very serviceable joint may be obtained by the latter method; but as the line of division of the bone runs below the tuberosities, rotation is practically lost.

In resections of the head of the humerus the writer employs the Kocher method, which consists of a curved posterior incision with a chiseling off of the spine of the scapula. It gives a free exposure of the joint, the function of the deltoid and the other shoulder muscles remains good, and subluxation of the upper end of the humerus toward the coracoid process is prevented. He employed it in a case of subcoracoid dislocation of the right shoulder, unreduced seven weeks after the accident. The right arm and hand were apparently paralyzed, although there were no considerable disturbances of sensation. The elbow was rigid in a right-angle position. An attempt to reduce the dislocation under ether was unsuccessful. By the Kocher method the shoulder-joint was exposed and opened. The dislocation was easily and quickly reduced by the use of a strong resection hook, which was aided by a large lever with a spoon-shaped end. The acromion was fastened in position with sutures. Three days after operation passive movemnets and the use of electricity were begun. The wound was completely healed in seven days, but the symptoms of paralysis disappeared slowly. Ten weeks after operation the patient could elevate his arm to a level with the shoulder. Passive movements in the shoulder were completely free, and he could make a fist. Pronation and supination at the elbow were possible. Active extension, however, was only slight. Madelung (Archiv f. klin. Chir., Bd. xc, S. 1126, 1909).

Habitual dislocation has been cured by reefing the anterior portion of the capsule. Ricard advises the usual anterior incision between the deltoid and pectoralis, supplemented by a horizontal one along the clavicle and dissection back of the anterior part of the deltoid.

Thomas has got good results by narrowing the inner part of the capsule at the site of the rent.

The writer applies this term to a condition of weakness of the joint in which any moderate external or internal force is sufficient to throw the joint surfaces out of their normal position in respect to each other. Excluding cases in which the trouble is the result of syringomyelia, he describes 42 cases from the literature and some in his own experience. The only reliable means of treatment is surgical and the joint should be opened for extraction of any movable bodies and to correct the condition as indicated. Good results have been obtained by merely taking up a fold in the capsule to make it smaller. Dahlgren (Nordiskt Med. Arkiv, vol. xli, No. 1; Surg. Jour. Amer. Med. Assoc., Jan. 30, 1909).

The writer's own experience has shown that reduction of the size of the capsule answers the desired purpose completely, even when there are other complications. Complete and permanent success follows. It is unnecessary to act directly on the other parts of the joint. R. Wilmanns (Zentralbl. f. Chir., March 20, 1909).

The most successful way of treating this condition is by means of open operation. The writer abducts the arm as far as a right angle and makes a curved incision, 7 or 8 inches long, in the line of the anterior axillary fold. The lower edge of the pectoral muscles is retracted upward, and the axillary vessels and nerves are gently drawn inward; the anterior circumflex artery may have to be divided. The separation downward of the fibers of the coracobrachialis muscle obviates harmful traction on the musculocutaneous nerve. The arm is now rotated outward and the head of the humerus is thrust forward, bringing the subscapularis tendon into the floor of the space between the neurovascular bundle and the coracobrachialis. The capsule of the joint is then exposed by separation and division of the fibers of the subscapularis. From the anterior aspect of the capsule a large oval piece, 1.25 by 0.5 inch, is removed, its long axis lying transversely to the fibers of the capsule. Foreign body or other abnormity of the joint cavity may thus be discovered and corrected. The incision in the capsule is then closed by formaldehyde solution gut sutures, and that in the tendon of the subscapularis is similarly repaired. The wound is closed without drainage, and the arm is fixed to the side for eight days. The sutures are then removed and passive and active movements are begun in all directions except abduction. At the end of the third week movements of abduction are started. The results of this method are excellent. Telford (Lancet, Aug. 3, 1912).

Dislocations of the elbow stand second in order of frequency, and are most common in persons under 25. Among the great variety of forms of dislocations of both bones, the backward are by far the most frequent.

The divisions and subdivisions are as follows:—

- Dislocation of Both Bones of the Forearm
  - 1. Dislocations backward:
    - and outward.
    - and inward.
  - 2. Lateral dislocations:
    - Incomplete
      - inward.
      - outward.
    - Complete — outward.
  - 3. Forward dislocations:
    - Incomplete (first degree).
    - Complete (second degree).
    - With fracture of the olecranon.
  - 4. Divergent dislocations.
    - Anteroposterior.
    - Lateral.
- Dislocations of Ulna Alone
  - Backward and Upward
    - Incomplete (first degree).
    - Complete (second degree).
  - Backward and Outward (behind the radius).
  - Inward (one case).
- Dislocations of the Radius Alone
  - 1. Backward.
  - 2. Outward.
  - 3. Forward.
  - 4. By elongation (the subluxation of children).
  - 5. With fracture of the ulna.

Dislocations of Both Bones Backward.—The inward and outward subvarieties are of no practical importance.

Symptoms.—The elbow is swelled and partly flexed. The olecranon may be felt displaced backward from the epicondyles and the head of the radius may be recognized behind the external epicondyle as a bony point which rotates with the forearm. The trochlear surface may be prominent in the bend of the elbow; the tendon of the biceps behind. Passive flexion and extension are moderate. There is abnormal lateral mobility in full extension.

The cause is most commonly a fall upon the outstretched hand forcing the two bones backward. The coronoid process of the ulna is either broken or lifted over the trochlear surface by hyperextension or by abduction, which increases the normal outward deviation of the forearm and a twist which swings the process downward and then backward.

Pathology.—The internal lateral ligament is torn, and the external one either torn or stripped away with the periosteum from the external condyle. Hence, in old dislocations reduction is effectually prevented by the mass of callus that forms beneath this elevated periosteum behind the external condyle. The front of the capsule is torn, the epitrochlea (internal epicondyle) may be broken by muscular pull, or the muscles attached to it may be ruptured. Fractures of the head of the radius and coronoid process are rare. The latter, however, does not interfere with the action of the brachialis anticus, as that muscle is attached to the base of the process: a part not interested in the fracture.

Treatment.—Forcible flexion is to be condemned as unscientific and less likely to succeed than pressure on the dislocated bones combined with traction of the forearm in full extension or hyperextension. Usually the dislocation is easily reduced. Sometimes anesthetics are necessary. After reduction the limb should be immobilized by bandages and a sling for about three weeks, after which massage and mild active motion will gradually remove the stiffness. Early passive motion will not hasten the result, and may even increase the excessive production of callus, which, in children, sometimes goes on even after reduction, and may cause serious limitation to the motion of the joint.

> In old-standing dislocations of both arm bones backward, reduction without a cutting operation is very rarely successful, and is often attended by very serious injury to the bones, especially in young subjects. Section of the olecranon allows easy reduction, and the fixation of the detached piece by a screw gives an ideal result. Operation from the posterior aspect of the joint is anatomically sound, as all the important structures, except the ulnar nerve, lie in front separated from the area of work by the brachialis anticus. No lateral incisions can give the power to deal with a shortened triceps, which will prevent reduction no matter how freely the lateral ligaments are divided. Fixation by a screw instead of by wiring saves much delay and avoids undue exposure of the periarticular tissues. M'Ardle (Dublin Jour. of Med. Sci., March, 1912).

Lateral Dislocations.—Incomplete dislocations in either direction are said to be frequently overlooked or mistaken for fractures. The cause of lateral dislocations is usually a fall upon the hand by which the normal outward angle at the elbow is increased by tearing of the internal lateral ligament and a downward movement of the ulna, directly away from the trochlea. The head of the radius then glides either outward or inward, as the case may be, the ulna accompanying.

In incomplete inward dislocations the forearm is pronated and slightly flexed, its long axis parallel to and a little to the inner side of that of the arm. The olecranon and external condyle are prominent, and the head of the radius can be felt displaced inward, resting below the trochlea (the greater sigmoid cavity of the ulna embraces the epitrochlea). Flexion and extension are but little interfered with. Reduction is made by traction and direct pressure. In unreduced cases there is very little disability, and operative interference is probably inadvisable.

Incomplete Outward Dislocations.—The forearm is pronated and slightly flexed, and its long axis is to the outer side of and parallel to that of the arm or else in abduction. The ulna is displaced so that the central ridge of the greater sigmoid cavity has passed beyond the outer rim of the trochlea; the radius lies partly below or entirely beyond the external condyle. The internal condyle and olecranon are prominent.

Treatment.—The ridge of the sigmoid cavity must be unlocked from the groove between the trochlea and capitellum. This is done by traction or hyperextension (or by abduction, if the head of the radius rests below the external condyle and can be used as a fulcrum). Then the bones are pushed easily into place. The broken epitrochlea may lodge in the groove of the trochlea and effectually prevent reduction. Even if the dislocation be not reduced, the joint may be quite useful.

Complete outward dislocation occurs in three forms. In the simplest form the bones of the forearm are displaced directly outward, the inner edge of the olecranon resting against the outer side of the external condyle. If, now, the forearm is flexed and strongly pronated, the second form (subepicondylar) is produced, in which the anterior surface of the ulna looks inward and its sigmoid cavity embraces the outer side of the external condyle, while the radius lies above it, with its head in front of the epicondylar ridge. In the third form (supraepicondylar) the dislocated bones are moved still farther upward and backward, so that their articular surfaces lie external to and behind the supinator ridge. Reduction is usually easy, owing to the extensive laceration of the ligaments; but, even if unreduced, the elbow remains fairly strong and mobile.

Forward Dislocation.—This rare injury is usually caused by direct trauma at the back of the flexed elbow. The olecranon was broken in about a third of the cases, and in such the violence is received on the posterior surface of the ulna. If this is the case, the ulna and radius are displaced forward and upward in the anterior surface of the humerus; but, if the olecranon remains intact, it may rest on the trochlea, or, the triceps being torn away, it may pass to the front of the humerus. Reduction by traction appears to have been easily accomplished.

Divergent Dislocations of the Radius and Ulna.—In the anteroposterior variety the ulna lies behind and the radius in front of the humerus; in the transverse the ulna is displaced inward and the radius outward. The usual cause seems to be abduction followed by internal rotation and impulsion. Reduction has failed in one-fourth of the cases.

Dislocation of the Ulna Alone.—The forearm is usually extended and adducted. Flexion is painful; rotation free. The trochlea is prominent in front and the olecranon behind, while the head of the radius remains in place. The cause of the injury appears to be hyperextension or abduction, followed by adduction and inward rotation. The rational method of reduction is by supination, abduction, and hyperextension (von Pitha).

Dislocation of the Radius Alone.—Of the dislocations backward, outward, and forward the last is the most frequent, being, in fact, of not unusual occurrence in connection with a fracture of the shaft of the ulna from a fall upon the hand. The head of the bone is displaced upward in front of the external condyle. The orbicular and anterior ligaments are torn. Abduction is possible, while supination, flexion, and adduction are all limited. Adduction and pressure appear to be the best methods of reduction; but the orbicular ligament may be interposed and require operative interference.

The backward and outward dislocations are very rare. They necessitate a fracture of the ulna or a rupture of the interosseous membrane.

The downward dislocation (dislocation by elongation, subluxation of young children) is of frequent occurrence. The clinical history is quite characteristic: a child, usually under 3 years of age, is pulled by the hand; it cries out, and refuses to use the limb, which hangs with the forearm partly flexed and pronated. The region of the head of the radius is sensitive to pressure, and sometimes an interval can be felt between the radius and the condyle. All passive motions, except supination, are free. On forcible supination a slight click may be felt and the symptoms are at once relieved. Duverney's theory of downward displacement with interposition of the annular ligament is most in accord with the facts.

In recent cases secure reduction of the dislocated radial head, by arthrotomy and capsulorrhaphy if necessary. As Kirmisson says, in such injuries the dislocation is everything, the fracture is nothing. When reduction is secured the fracture almost invariably will fall into good position. If it does not, it may be fixed by a suture or plate. In old cases with the ulna united attempt reduction of the dislocation by arthrotomy and retain the radius in place by capsulorrhaphy. If reduction after arthrotomy proves impossible, as it may if the ulna has united in bad position, it is better to excise the head of the radius than to interfere with the ulna, unless the deformity in the ulna is very extreme. In such cases osteotomy of the ulna may be done. In old cases with non-union of the ulna expose the ulnar fracture first, and after freeing the fragments secure reduction of the dislocation by arthrotomy if necessary, including capsulorrhaphy; then treat the ulnar fracture as if no dislocation had existed. In cases with musculospiral paralysis excision of the radial head failed to secure a good result in one case (Zschock), and there is no evidence that reduction and capsulorrhaphy would not have been successful in two others (Albertin, Kammerer) in which excision was done. A. P. C. Ashhurst (Annals of Surg., Oct., 1912).

Old Unreduced Dislocations of the Elbow.—Adhesions and new bone formation very soon immobilize the joint. If this immobilization occurs in extension, the position may be improved by forcible flexion, with or without fracture of the olecranon. A more accurate method, however, and one likely in many cases to afford fairly good functional results, is arthrotomy. The chief obstacle to reduction will be found to be the new bone formed at the back of the external condyle. This may be removed and adhesions divided through two lateral incisions.

The writer has treated 34 old dislocations of the elbow. In the first cases he attempted reduction without operation. In no case did he succeed when the dislocation was more than three weeks old. The operations which followed showed such anatomical changes as to render reduction impossible without exposure of the body ends of the joint. He now operates on any case that is more than three weeks old. Dollinger (Deut. Zeit. f. Chir., Bd. c, S. 38, 1909).

Dislocations of the Lower Radio-Ulnar Joint.—The ulna is spoken of as the dislocated bone. It may be dislocated forward or backward. The latter variety is caused by exaggerated pronation, and the former by direct trauma. Both are easily reduced.

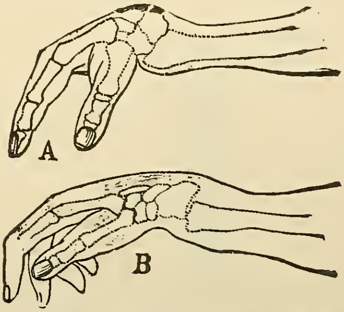

Fig. 11.—Diagrammatic, to indicate the deformity in *A*, dislocation of the wrist backward, and *B*, Colles's fracture of the radius. (*Stimson.*)

Dislocations of the Carpus from the Radius.—These may be complete or incomplete; forward, backward, or outward. In the incomplete form the cuneiform maintains its relations to the triangular fibrocartilage, while the scaphoid and semilunar are dislocated from the radius. In one case the semilunar alone was not displaced (backward). These dislocations may be complicated by fracture of the anterior or posterior ("Barton's fracture") lip of the radius; but this in no way complicates the treatment and is a purely secondary matter.

The more common Colles fracture of the lower end of the radius was long confounded with backward dislocation. The differential diagnosis is easily made by attention to the relations of the styloid process of the radius with that of the ulna and with the projecting mass on the back of the wrist (Fig. 11). Reduction in either case is made by dorsal flexion and direct pressure, and after reduction the differential diagnosis is easy. The spontaneous forward dislocation of Madelung occurs slowly in adolescents as the result of absorption of the anterior part of the articular surface of the radius. The ulna is abnormally prominent; dorsal flexion is limited.

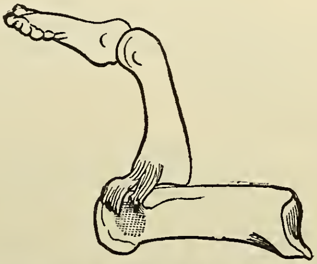

Fig. 12.—Simple complete dislocation of the thumb. (*Farabeuf.*)

Madelung has been shown to have been in error, in that there is no luxation, but a diaphyseal or epiphyseal incurvation of the radius. The disease is, therefore, a curved radius. The radiocarpal connection remains normal. The writer reports a case in which the radial curve existed on both sides, much more marked on the left than on the right. The deformity had its origin a year before, and during the same time there developed a tubercular arthritis of the left tibiotarsal joint with fistula, which has been cured. The patient entered the hospital for a right coxalgia, which kept him in bed for six weeks. All these disturbances have followed pseudorheumatic articular pains, which have lasted a year and have presented their maximum intensity at the wrists. The patient is tuberculous, the tuberculosis being of the articular form. The skiagram shows that the lesions occur only at the inferior diaphysoepiphyseal junction. After the pseudorheumatismal beginning, the tubercular lesions localized themselves at the left tibiotarsal articulation and the right hip. Then, simultaneously, there developed a double radial curve at the wrists. Marson (Arch. gén. de chir., vol. ii, p. 472, 1908).

Dislocation of the Carpal Bones.—Dislocations have been reported of each of the carpal bones, except the cuneiform. If the bone cannot be replaced or causes annoying symptoms, it had better be removed.

Case of dislocation of the semilunar bone in a young man, resulting from an accident. The disturbances were so severe that he was unable to use his hand and, after failure of persevering conservative measures, Ipsen removed the semilunar bone as the dislocation constantly recurred after reduction. This put an end to the disturbances at once without impairment of function. Ipsen (Hospitalstidende, Feb. 10, 1909).

A few dislocations of the second row of carpal bones upon the first have been reported.

Carpometacarpal Dislocations.—The first metacarpal is the one most commonly dislocated; the dislocation is incomplete and usually backward. The base of the dislocated bone forms a distinct prominence on the back of the hand; this is readily reduced, but as readily recurs. To prevent recurrence, extension of the finger (and also abduction, if it be the thumb) and direct pressure on the head of the bone must be maintained by a dorsal splint for one or two weeks.

Dislocations of the Thumb and Fingers.—*Metacarpophalangeal Dislocations of the Thumb.*—Lateral (one case) and forward dislocations present no especial points of interest. The latter are easily reduced by hyperflexion and traction. Backward dislocation may be incomplete, complete, or complex. Incomplete backward dislocation may be produced voluntarily by many young persons. It is reduced at will. In the complete form the phalanx is carried backward and upward on the dorsum of the metacarpal, usually by forced extension; the anterior ligament is torn away from the metacarpal bone and drawn backward with its sesamoid bones along, and even past, the articular surface of the head of the metacarpal, while the tendon of the long flexor slips to one side of the head, usually the inner, although it may exceptionally remain in place. The first phalanx is in extension at a right angle, the terminal phalanx in flexion, and the head of the metacarpal prominent in the thenar eminence (Fig. 12).

In the complex form (produced from the complete by forced flexion of the thumb) the glenoid ligament, and the two sesamoid bones with it, are turned upward so as to lie between the phalanx and the head or dorsum of the metacarpal. The thumb is in straight extension, parallel and posterior to the metacarpal; its base can be felt as a prominence behind, and the head of the metacarpal protrudes in front. The sesamoid bones stand at a right angle to the articular surface of the phalanx, and cannot be folded under it, thus offering a great—often insurmountable—obstacle to reduction. The essential point of reduction, therefore, is to avoid the transformation of the complete into the complex form. The extension must be maintained or even increased and the thumb pressed bodily downward until the anterior edge of its base, following the glenoid ligament, overlaps the articular surface of the metacarpal, when it can be turned into place by flexion. If this fails, a combination of rotation with the downward pressure may succeed: a sort of unbuttoning of the head of the metacarpal from the grasp of the glenoid ligament and the attached heads of the short flexor. If, however, the dislocation has become complex by the interposition of the glenoid ligament, the same method may yet succeed; but much more forcible downward traction is necessary to carry the edge of the ligament over the end of the metacarpal bone ahead of the phalanx before instituting flexion. If all manipulations fail, the joint must be opened through a longitudinal anterior incision, and the center of the glenoid ligament nicked deeply enough to allow it to be drawn over the head of the metacarpal, after which the dislocation may be readily reduced.

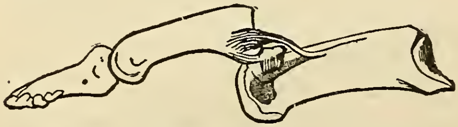
Fig. 13.—Complex dislocation. (*Farabeuf.*)

Metacarpophalangeal dislocations of the fingers present the same features as those of the thumb, save that they usually have no sesamoid bones.

Dislocation of the phalanges may occur in any direction. Reduction is usually easy, though it is possible that the thick anterior ligament may be interposed, as in the metacarpophalangeal joint.

Dislocations of the Pelvis and Coccyx.—Dislocation of the pubic and sacroiliac symphyses occurs in connection with fracture of the pelvis, the symptoms and treatment of which it does not materially complicate.

The coccyx may be dislocated forward or backward. The pain is usually intense. Diagnosis and reduction are effected by rectal touch. The tendency to recurrence can only be remedied by excision of the bone.

Dislocations of the Hip.—These form from 2 to 10 per cent. of all dislocations; they occur at all ages and are more common in men than in women. The head of the femur may leave its socket in any of the four principal directions, after which it assumes various positions by secondary displacement. In "typical" dislocations the Y-ligament remains untorn and determines the characteristic attitude of the limb (Bigelow). Compound dislocations are rare. The varieties are as follows:—

- Dislocations Backward
  - "Typical" dorsal (comprising the iliac and "ischiatic," and those "upon the dorsum ilia" and "into the ischiatic notch").
- Dislocations Backward
  - Anterior oblique.
  - Everted dorsal (comprising the "supraspinous" and some of the "supracotyloid").
- Dislocations Downward and Inward
  - Obturator.
  - Perineal.
- Dislocations Forward and Upward
  - Suprapubic
    - Ilio-pectineal.
    - Pubic.
    - Intrapelvic.
- Dislocations directly upward (supracotyloid or subspinous).
- Dislocations downward on the tuberosity of the ischium.

Backward Dislocations.—The dorsal form is by far the most common of the dislocations of the hip. The thigh is adducted, rotated inward, and more or less flexed; so that the knee rests upon the front of the opposite thigh when the patient is recumbent, and there is apparent shortening (Fig. 14). The upper and outer part of the thigh is broadened, and the trochanter is above Nélaton's line (a line drawn from the antero-superior spine of the ilium to the tuberosity of the ischium). The head of the femur may be obscurely felt in the buttock.

The actual shortening cannot easily be determined on account of the difficulty of placing the two limbs in symmetrical positions. Voluntary movements are lost; passive flexion and adduction alone are possible.

The characteristic position and limitation of motion readily distinguishes the dislocation from a fracture of the neck of the femur.

Etiology.—The dislocation is usually produced by violence transmitted along the shaft of the femur while the thigh is flexed, adducted, and rotated inward, or the head of the bone may be thrown out of place by exaggerated adduction, inward rotation, and slight flexion, or, again, the dislocation may result secondarily from an obturator dislocation by the same three motions.

Pathology.—The head of the bone usually tears through the capsule low down behind, passes below and then upward behind the obturator, and rests finally on that muscle close behind the acetabulum, or, more rarely, it leaves its socket higher up, pushes the obturator ahead of it outward or upward, and lies on the edge of the acetabulum itself. The capsule is irregularly torn behind, the ligamentum teres is ruptured, the quadratus femoris and gemelli are usually torn, the two obturators and pyriforms less frequently. Rarely the head of the bone rests on the great sciatic notch or the dorsum ilii. The edge of the acetabulum may be broken.

Treatment.—The surgeon must endeavor to relax the Y-ligament and other untorn portions of the capsule, to bring the head of the bone opposite the rent in the capsule (if necessary), and then to lift or pry it into place. To do this the patient is laid flat on his back and the pelvis steadied by an assistant or by the surgeon's foot. The patient's knee is then flexed at a right angle, the thigh rotated inward and flexed to or a little beyond a right angle, and then lifted bodily upward, rotated a little outward, and extended in abduction. The lifting and outward rotation should replace the bone with a distinct jump.

Or the patient may be laid on his face on a table whose edge comes just above the groin so as to leave the lower extremities dangling. The sound limb is now held horizontally by an assistant, and the dislocated one allowed to hang vertically downward. The surgeon grasps the ankle of the dislocated limb, flexes the knee to a right angle, and, while diverting the patient's attention, swings the limb gently from side to side. Under the influence of gravity the muscles soon relax and the bone may slip into place of itself or aided by a sharp, quick pressure downward on the calf.

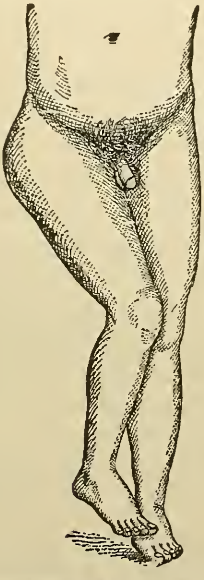

Fig. 14.—Dorsal dislocation of femur. (*Cooper.*)

If these methods fail, ether should be administered and reduction attempted several times by the first method. Failing again, try traction in slight flexion and adduction, aided by direct pressure on the great trochanter.

If the limb is too strongly flexed or too soon rotated outward the dorsal dislocation may be transformed into a thyroid one. If this occurs, the dislocation must be restored to its original form by reversing the movements: flexion in abduction and outward rotation, followed by adduction and rotation inward.

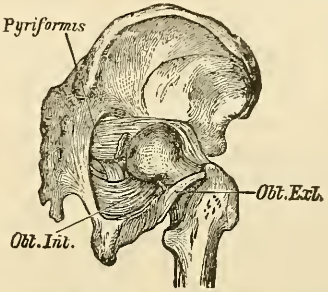

Fig. 15.—Dislocation below, and then behind and above, the obturator internus. (*Stimson.*)

In reviewing the ultimate results observed in 21 cases of hip luxation, some reduced by ordinary methods soon after the accident, others treated later by open operation, the writer concludes that the late prognosis in these cases is not entirely favorable. Although occasionally the subsequent trouble may arise from osseous abnormalities existing before or as the result of the accident, and which might have been avoided by routine use of the X-rays in these cases, the disturbance is usually due to imperfect restoration of the soft parts surrounding the joint. In adults, one should always be apprehensive of a posttraumatic deforming arthritis, which may appear at a long interval after the accident. The best way of preventing this and other untoward results is to keep all these patients under treatment, after the dislocation, for a longer time than has hitherto been the custom. In reducing hip luxations, he advises the following maneuver, which permits of easy reduction, even where the patient's limb is unusually massive: With the patient anesthetized and lying on a mattress, the thigh is flexed to liberate the femoral head, and the operator's knee placed under that of the patient. Holding the patient's leg below the knee and at the ankle, the operator then applies force to it just as a laborer would lift a heavy shovelful of earth. Roux (Revue méd. de la Suisse Romande, Jan., 1913).

Everted Dorsal Dislocations.—If the outer branch of the Y-ligament is ruptured, the limitation to abduction and outward rotation is, in great part, removed, and the head of the bone is free to rise higher than before. Hence, when this rupture occurs, if the head remains behind the acetabulum only slight flexion and adduction persist, while, if it has moved upward and forward near to or above the anteroinferior spine of the ilium (in which position it can be felt), there will be extension, abduction, and slight outward rotation: the so-called everted dorsal. Reduction is effected by converting the dislocation into the common dorsal form and treating it as such.

Anterior Oblique Dislocation.—In Bigelow's one reported case the head of the bone was high above the acetabulum and the limb crossed the opposite thigh, everted, and with the knee extended. Reduction as for everted dorsal dislocation.

Dislocations Downward and Inward.—In both the obturator—or thyroid—and perineal varieties the head escapes through a rent in the lower and inner part of the capsule to lodge on the obturator foramen, or to proceed farther and rest on the perineum. In either case the limb is flexed, abducted, and rotated outward. It cannot be extended and can only be adducted after flexion. The limb is shortened, the trochanteric region flattened, and adductors tense. The head of the femur may sometimes be felt on the foramen, always if it is in the perineum, in which latter case the abnormality of the position of the limb is much greater. Several patients are reported to have walked immediately after receiving a thyroid dislocation.

The common cause is violence received on the back of the pelvis while the thigh is somewhat flexed and abducted; but it may be extreme abduction alone. In perineal dislocations the laceration of the soft parts must be extensive.

Reduction is made by flexion of the hip to a right angle, traction with adduction, and then inward (or outward) rotation while lowering the knee. Manipulation may succeed with no rotation at all.

Dislocations Upward and Forward, and Inward and Forward (Suprapubic).—The limb is extended, markedly everted, and slightly abducted. The head of the femur is commonly to be felt in the groin (iliopectineal form) or may be above the pubes. The psoas-iliacus and the great vessels are stretched across the head or may be ruptured. The head of the bone may have left the socket at its upper and inner part by hyperextension, or by abduction and outward rotation, or the dislocation may be secondary to an obturator dislocation.

Reduction.—The head is to be drawn downward past the pubic ramus by direct traction in the axis of the limb as it lies; then flexion is instituted while pressure is made against the head to prevent its moving upward again; and, finally, inward rotation replaces the bone.

Dislocations Directly Upward (Supracotyloid).—In the few recorded cases the head had been forced directly upward and lay just beneath the anteroinferior spine of the ilium. The limb was everted and abducted. Some of the patients have been able to walk with a limp.

These cases bear a close resemblance to everted dorsal dislocations. No definite rules for reduction have been laid down.

Dislocation Downward upon the Tuberosity of the Ischium.—This dislocation is very rare because of the ease with which it may be converted into a dorsal or thyroid dislocation. The thigh is sharply flexed and abducted. Reduction is easy by traction in flexion.

Complications of Dislocations of the Hip.—Compound dislocations are very rare.

Injury to the femoral vessels may occur in forward and inward dislocations.

Fracture of the neck of the femur is usually caused by overzealous attempts at reduction. Ankylosis with the limb in a favorable position is the best that can be hoped for, except possibly in the young, when excision of the head of the bone may give some useful motion.

> By central dislocation of the femur is meant fracture of the acetabulum with dislocation of the head of the femur into the pelvic cavity. Most cases of this character are reported under the head of fracture of the acetabulum. From the writer's viewpoint, the presence of the femoral head in the pelvic cavity is the most important feature. Halstead (N. Y. Med. Jour., Nov. 13, 1909).
>
> In reporting a case in a young woman five months pregnant when the head of the femur was driven into the pelvis by a fall from a wagon, the writer refers to 31 cases on record occurring in pregnant women. To these he adds a list of 64 cases of simple and compound fracture of the floor of the acetabulum and 44 others of central luxation. It is important to refrain from bearing weight on the limb until after reduction and retention of the femur in its normal place. One should not attempt to reduce the head of the femur by manipulations through the rectum, although this is advisable to reduce the fragments of bone after the head has been restored to place. A plaster cast extending above the costal arch is necessary to retain the parts in the desired position, the hip being flexed and in adduction, with longitudinal extension, the technique for which is described in detail. The patient must stay in bed for two or three months; premature use of the limb will annul or render impossible good results. Henschen (Beiträge z. klin. Chir., March, 1909).
>
> The symptoms of central dislocation of the femur are very similar to those seen in impacted fracture of the neck of that bone: (1) outward rotation of the femur; (2) sinking of the trochanter or its approach toward the median line; (3) shortening; (4) restricted motion; neither flexion, adduction, abduction nor rotation is normal. The limitation in the arc of rotation of the neck of the femur is striking; (5) presence of the femoral head in the pelvis. The diagnosis can be made from impacted fracture of the neck and from all other injuries which it resembles except certain other fractures of the pelvis, by feeling through the rectum, or seeing, by means of the X-ray examination, the head of the bone projecting into the pelvis. From certain other fractures of the pelvis with projection of the head into the pelvic cavity, the diagnosis can be made only by means of the Roentgen-ray or by exposure by operation. Reduction should be attempted as advised by the usual methods, namely, by traction outward and downward in the axis of the neck of the femur. Failing in these, the dislocation should be reduced by open method. Vaughn (Surg., Gynec. and Obstet., Sept., 1912).

Treatment of Old Unreduced Dislocations.—Both forcible reduction and reduction by arthrotomy have yielded, as a rule, only moderate functional results and also show a large percentage of mortality. The results are not materially better than those got by resection of the head or by osteotomy. At present, except in experienced hands, the object sought should simply be to improve function by a change in the attitude of the limb by the simplest means.

For practical purposes, all regular dislocations of the hip are, in reference to the acetabulum, either posterior or anterior. Whatever be the dislocation, an imaginary arrow on the exposed surface of the lower leg pointed toward the flexed knee will, if the Bigelow method of replacement is used, remind the surgeon during the flexion whether to make the knee describe an inward or an outward arc. Monks (Boston Med, and Surg. Jour., Feb. 23, 1911).

Dislocations of the Knee.—These occur rarely and, in order of frequency, forward, backward, outward, inward, and by rotation. The dislocation is frequently compound, and the prognosis rendered much more grave by a complicating injury to either of the popliteal nerves or to the popliteal vessels. Even if, after reduction, pulsation reappears in the arteries of the foot, gangrene may supervene from thrombosis caused by laceration of the inner coats of the artery.

Case of **external** dislocation of the tibiotemporal joint, a still rarer form of a rare dislocation. The patient was injured by strikers during a labor riot, and the dislocation was simple and not complete. There was a fracture of the external tuberosity of the tibia. There was no injury to the vessels and the reduction was easily accomplished. Ten days later the man died of lobar pneumonia and on opening the knee-joint there was an effusion of blood and comminuted fracture of the outer part of the head of the tibia with rupture of the external lateral ligaments and the anterior ligament, while the internal was only partially ruptured. The anterior crucial ligaments were torn, the posterior intact. R. H. Fowler (Jour. Amer. Med. Assoc., Dec. 30, 1911).

Forward dislocation may be complete, or, more commonly, incomplete. When complete, the tibia may be displaced some distance upward over the front of the condyles. If the dislocation is compound, the wound is posterior and transverse. The cause is direct violence or hyperextension of the knee. Reduction is easily made by traction and pressure.

Backward dislocations may be complete or incomplete. The leg is usually either extended or hyperextended, and may be deviated to one side. The patella may be dislocated outward. The usual cause is direct violence. Reduction is effected by traction and pressure. Even without reduction a fairly useful limb has resulted in several cases.

Lateral dislocations are outward or inward, complete or incomplete. The patella is usually deviated toward the side of the dislocation. The incomplete form is usually caused by abduction or (inward) by adduction. Reduction by traction and pressure. Dislocation by rotation is said to be incomplete when one condyle revolves around the other, complete when both revolve around a central axis. There may be additional backward or outward displacement. The rotation is said to be outward or inward according to the direction in which the toes turn. Reduction is easy. All knee dislocations should be kept immobilized for several weeks after reduction.

Analysis by the writer of the 21 published specimens of congenital hyperextension shows the pathological lesion to consist in a subluxation of the tibia forward and upward on the femur. As a consequence of this position the extensors of the knee and the anterior portion of the capsule are shortened, the flexors are frequently dislocated forward so as to be converted into extensors, the gastrocnemius may be displaced downward, the patella usually displaced upward, the anterior portion of the femoral condyles is usually flattened and forms an articular surface which, running from below upward and forward, encroaches on the facies patellaris or entirely replaces it, and in some cases there is anteversion of the femoral epiphysis. The deformity is due to an extension of the legs *in utero*, which, owing to normal intra-uterine pressure, is converted into hyperextension. The ultimate cause of the extended position is unknown.

Treatment should be begun at birth and consists at first in manipulation, with narcosis and apparatus if necessary, to reduce the subluxation. In case repeated attempts to reduce are unsuccessful, open operation is indicated. The type of operation depends first on the obstacles to reduction—usually the contraction of the quadriceps and the anterior capsule; second, the factors, ligamentous, bony or muscular, tending to cause a recurrence of the subluxation. Special care must be taken to restore the normal mechanical relationships of the gastrocnemius, since it exercises an important function, hitherto not generally recognized, in preventing hyperextension. The poor therapeutic record in patients over 2½ months old (only 33 per cent. cures) indicates the necessity for the most careful study of the pathological lesions present, so that, if bloodless reduction fails and operation be attempted, the normal relations, muscular and ligamentous as well as bony, can be restored. Mayer (Amer. Jour. of Orthop. Surg., Feb., 1913).

Dislocation of the Semilunar Cartilages.—Either cartilage may be detached from any of its ligamentous attachments, and so displaced in any direction, or it may be lacerated.

The symptoms are those of any loose body in the joint, sudden painful locking, usually after some given movement. The displacement may be recognized by palpation along the articular edge of the tibia. The cause of displacement is a dislocation, a sprain, excessive rotation, or flexion.

Treatment.—The locking may be relieved by forcible manipulation or by pressure upon the displaced cartilage. Various braces have been devised to prevent recurrence, either by opposing the displacement directly or by preventing the motion which occasions the displacement. These methods failing, the cartilage may be removed or sutured into place through an incision alongside of the ligamentum patellæ.

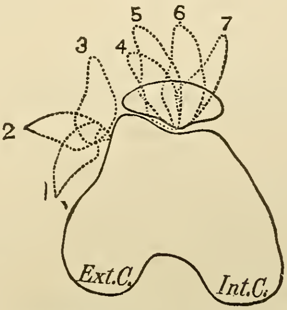

Fig. 16.—Diagram of the various dislocations of the patella. (*Stimson.*)

Dislocation of internal semilunar cartilage of the knee occurs most commonly when an individual, while standing solidly on one foot, *e.g.*, on a step-ladder or chair, makes a quick move or executes inward rotation at the knee. The internal condyle of the femur, pressing against the cartilage, displaces it inward, rupturing the coronary ligaments.

In treating this accident, the writer fits a piece of sole leather about 4 inches long and 1¾ inches wide to the inner side of the knee. By first soaking the leather in water and whittling the edges so that it is smooth, it may be molded into shape. It is fastened over the cartilage by adhesive straps—two up and down, one horizontally and one oblique—and covered with a fairly firm bandage. The patients may walk as usual, though for the first three or four days they complain of some local soreness. The bandage is renewed every ten days. After about three such treatments, the patients are well and only a bandage need be used. The irritation of the leather probably causes an aseptic adhesive inflammation to be set up between the loosened cartilage and bone, this taking the place of the ruptured coronary ligaments. G. Chandler (Jour. Amer. Med. Assoc., Oct. 28, 1911).

Dislocations of the Patella.—The patella may be dislocated outward or inward, or rotated around its long axis, or the two forms may be combined. Displacement upward or downward is purely secondary to rupture of the ligamentum patellæ or the quadriceps tendon, and need not be here considered.

Outward dislocation is complete or incomplete, and accompanied by various degrees of rotation (Fig. 16: 1, 2, and 3). The patella is readily felt in its new position, though it may be difficult to determine whether the outer or the inner border is directed forward. Muscular action and direct violence are the causes of the dislocation, and hydrarthrosis and ligamentous weakness are predisposing causes. The fibrous expansion of the vastus internus is ruptured, and the muscle itself may be more or less torn. Reduction is made by direct pressure during extension of the knee and flexion of the hip.

Incomplete dislocations are those in which, during extension or flexion, the patella moves outward on to the external condyle.

Outward, Edgewise, or Vertical Dislocations (by Rotation).—In these the patella is moved outward and its inner edge backward into the intercondylar groove; so that its articular surface looks outward and more or less forward, or completely forward (Fig. 16: 4 to 7). The causes and treatment are the same as for outward dislocations.

Inward dislocations present the same features, *mutatis mutandis,* as the outward, but they are much less frequent.

Habitual dislocations are usually the result of some deformity, such as genu valgum. They are controlled by correcting the original deformity, or by apparatus, or by tightening up the loose lateral ligaments (by operation).

In the family described by the writer, bilateral luxation of the patella was observed in the grandfather, in the father, in his sister and one of his five brothers, and in the son and daughter. Wrede (Med. Klinik, Jan. 1, 1911).

The writer recommends the following method: The semitendinosus tendon is isolated and cut as near its insertion as possible. A strip of the ligamentum patella is also detached and brought inward to meet the semitendinosus tendon. Those were then united to suture to each other and also to the inner fascial capsule of the knee, which is then plicated by several sutures. The leg is kept fully extended on a posterior splint for four weeks. The patella is prevented from becoming displaced outward during flexion. Robertson (Surg., Gynec. and Obstet., April, 1912).

Dislocation of the Fibula.—The upper end may be dislocated outward and forward, or backward, or upward. These dislocations are all rare. The first form seems to be caused by muscular action of the long extensors of the foot; the second (in more than half the cases) by action of the biceps, and the third by an injury resembling Pott's fracture, in which the fibula, instead of being broken, is forced upward.

A complicating fracture of the tibia may exist. Recurrence is likely, although reposition is easy, and, hence, immobilization should be maintained for several weeks.

The lower end may be dislocated

backward. This is quite as rare as the dislocation outward in connection with Pott's fracture is common.

Dislocation of the Ankle (Tibiotarsal).—*Backward.*—By extreme plantar flexion the lateral ligaments are torn, the foot slips back, and the astragalus is caught behind the tibia. (Incomplete dislocation is a frequent accompaniment of Pott's fracture.) The malleoli may be fractured. The lengthening of the heel and shortening of the foot may only be determined sometimes by careful measurement.

Forward.—Rare. Caused by pressure on the heel or by exaggerated dorsal flexion.

Inward.—Two varieties. In the one the astragalus is pried out by supination and adduction, and the foot moved directly inward and forward; in the other (thought to be secondary to a backward dislocation) the foot is turned over so that its plantar surface faces directly inward. Reduction is easy.

Outward.—Appears always to be associated with Pott's fracture.

Subastragaloid Dislocations.—The other bones of the foot may be dislocated from the astragalus outward, inward and backward, forward, or backward. The first two are the most common. About 50 per cent. are compound. About 50 per cent. of attempted reductions have succeeded. Complicating fractures are not infrequent. Notwithstanding the persistence of the displacement, a good functional result may be obtained in some unreduced cases. Primary and secondary excision of the astragalus have given good functional results.

Dislocations of the Astragalus.—The varieties are forward, backward, outward and forward, inward and forward, and by rotation. There is frequently more or less rotation in connection with the other displacements.

Outward and Forward.—This is the most frequent form. The foot is adducted and inverted and the external malleolus prominent. The astragalus rests on the outer cuneiform and cuboid bones, or even on the fifth metatarsal. Its posterior part is still in contact with the articular surface of the tibia. Reduction by traction on the foot and pressure on the astragalus is usually easy, unless the bone is rotated.

Inward and Forward.—The foot is abducted and everted, and the astragalus lies in front or below the malleolus Reduction may be prevented if the tendon of the tibialis anticus embraces the neck of the dislocated bone.

Forward.—Very rare. The cases reported have no features in common.

Backward.—There may be lateral displacement. In about 50 per cent. of cases the bone was broken at the neck and only the posterior fragment dislocated. There may be flexion of the terminal phalanx of the great toe. Reduction was effected in one-third of the simple cases.

Rotatory.—Dislocation by rotation alone may take place about the vertical or transverse axis (in these latter there is always some displacement forward and inward) or about the anteroposterior axis.

> The cause of the dislocation of the astragalus is a very severe force, generally in the young and vigorous, transmitted from above downward against the astragalus, the foot being in a varus position and forced adduction. Reduction should be attempted early, to avoid necrosis of the skin stretched over the prominent astragalus. General anesthesia is necessary to relax the rigid muscles, especially the gastrocnemius. Flexion of the leg on the thigh is very valuable. The fear of ultimate necrosis

of the largely detached astragalus should not be regarded as a contra-indication to reduction. The increasing number of operative reductions of total dislocations of the astragalus prove that the nutrition does not become compromised. Pouzat, in 1884, in 31 cases of complete dislocation, showed 19 successful reductions. Trenel, Worms and Doeckel (Arch. gén. d. chir., vol. vi, p. 551, 1910).

Removal of the astragalus may be expected to give a good functional result.

Dislocations of the Tarsus and Metatarsus.—These are too rare and irregular for systematic description.

The writer found 15 cases on record of dislocation of Lisfranc's joint since Lenormant's complication of 96 cases in 1908, thus aggregating, with two personal, 113 cases. The luxation was total in 58. Reduction by manual pressure succeeded in only 35 per cent., but the patient got along well with the uncorrected total dislocation, while the outcome was most disappointing in the operative cases. Operative interference is liable to do harm ultimately rather than good in the total luxations, but when only a single bone is dislocated operative interference is justified and has always proved effectual. The foot is weakened by resection of the bone. Gruner (Deut. Zeit. f. Chir., Oct., 1910).

Lewis A. Stimson
and
James M. Hitzrot,
New York.

DISTOMUM. See Parasites, Diseases Due to.

DIURETIN, or **theobromine sodio-salicylate,** is a double salt of theobromine-sodium and sodium salicylate [$C_7H_7N_4O_2Na + C_6H_4(OH)COONa$]. Its chief constituent, theobromine, of which it contains about 50 per cent., is a dimethylxanthine, and is therefore closely allied to caffeine, which is trimethylxanthine. It occurs as a white, odorless powder, having a saline and somewhat alkaline taste, and has the advantage over pure theobromine of being soluble in water. Diuretin is hygroscopic and is decomposed when exposed to carbon dioxide or to acids; it should therefore be kept in well-closed containers. It is incompatible with chloral hydrate, phosphates, bicarbonates, ferric salts, and even traces of free acids. It is not official.

PREPARATIONS AND DOSE.—For diuretic purposes, the drug may be given in doses of 15 grains (1 Gm.) as often as five or even six times a day, in adults. In arteriosclerosis smaller doses should be employed: 8 grains (0.5 Gm.) three or four times daily. It may be given in water, but some simple flavoring agent, together with administration of the drug in syrup (not syrup of orange-peel or lemon, however) may be of advantage in that the slight alkaline taste will be disguised. It may also be given in milk. It should be taken between meals.

PHYSIOLOGICAL ACTION.—The drug is a powerful diuretic, acting especially by stimulation of the peripheral vasodilator nervous mechanism in the kidneys which results in increased caliber of the renal vessels and a markedly increased flow of blood through the organs. Although it is possible that theobromine acts in part by directly exciting the renal secreting cells, modern pharmacological work has lent no support to such an action, and the statement seems warranted, both from this work and clinical experience, that the drug causes little or no irritation in the kidneys. Gruenwald deems it probable that the glomeruli are chiefly influenced. Certain features of his experimental results, however, led him to conclude that a paralysis of the process of reabsorption in the kidneys—in regard to salts especially—also forms part of the action of the drug.

According to Hoffmann, Pawinski, and others, the diuretic effect in dropsy shows itself slightly in the first twenty-four hours after the initial dose of the drug. It becomes well marked after two days, and reaches its height in four or five days, when it may be so pronounced that 5 or 6 liters of urine are voided in the twenty-four hours. Theobromine preparations are superior to caffeine as diuretics in that the action is more pronounced and prolonged and is unaccompanied by symptoms of central nervous excitation.

It is by many considered superior to theophylline (theocin) in causing less gastrointestinal and nervous disturbance, and is certainly, in the average case, likely to cause a more prolonged diuretic effect; sometimes, however, theophylline will induce a more marked and prompt diuresis than theobromine.

In common with the other drugs of the caffeine group, diuretin causes an increase in the elimination of certain salts, especially sodium chloride and the phosphates. The nitrogenous constituents of the urine may also be increased, though to a less extent.

> Continued administration of diuretin will bring about an excretion of salt, even in rabbits whose food is poor in salt. If the administration be continued long enough, an intoxication will result, evident at first in reflex hyperexcitability, later in progressive paralysis leading to death. These symptoms disappear if salt is given, but other drugs have no effect. The specific action of diuretin, as far as the salt is concerned, is primarily upon the kidneys. The action of diuretin remains the same even if the renal epithelium has been injured by large doses of mercury. The parts chiefly affected by diuretin are the glomeruli. In experiments on animals with deficient salt, all remedies which dilate the renal vessels will cause increased excretion of salt. H. Fr. Gruenwald (Arch. f. exper. Path. u. Pharm., No. 5, 1909).

Upon the heart theobromine compounds exert the same stimulant action as caffeine. Upon the vascular system, however, they act differently, tending to dilate the peripheral vessels, as well as the coronaries and renal vessels. The blood-pressure does not fall, but may instead be slightly raised, owing to the augmented heart action (Haynes). The stimulant action of caffeine on the vasomotor center is wanting with theobromine; this is believed to account for the ease with which it maintains the kidneys in a state of increased secretory activity, no constrictor impulses reaching the renal vessels from the vasomotor center no matter what the dose of theobromine given.

> Report of experiments on dogs to determine the effect of theobromine sodiosalicylate on the blood-pressure. Intravenous injection of minute amounts (0.04 Gm. in a 6-kilo. dog) produced a very slight pressor effect. Somewhat larger dosage (0.1-0.2 Gm. in an 8-kilo. dog) produced little if any effect. A very slight increase over an amount which had no effect on the blood-pressure caused a distinct depressor effect. Larger amounts produced a correspondingly greater depression. Small amounts caused a moderate slowing of the heart rate while the large doses usually caused acceleration,—probably an attempt to overcome the fall of pressure. That the depressor effect is due to a peripheral (vascular) action was demonstrated by comparing the effect of injection of equal amounts of the drug before and after section of both vagi: A fall in pressure of 24 mm. occurred before and one of 62 mm. just after section of these nerves. The results suggest strongly that the relief given by theobromine in abdominal angina is due to splanchnic dilatation, the area of greatest peripheral vasodilatation. The effect on the blood-pressure seems to be of secondary importance, depending on the relative balance between cardiac activity and peripheral vasomotor tone. W. W. Hamburger (Interstate Med. Jour., June, 1911).

Theobromine appears to possess to a certain extent, in common with caffeine, the property of dilating the walls of the bronchioles when these are in a state of constriction, as in the acute asthmatic paroxysm. It slightly increases general muscular power. Rost found in the dog that from 10 to 30 per cent. of the large doses given could be recovered in the urine. A part of the theobromine ingested by any mammal appears to be demethylated to monomethylxanthine before excretion. According to Aubel, theobromine may be found in the urine of man six hours after a dose of diuretin has been ingested, and after twenty-four hours it has completely disappeared.

UNTOWARD EFFECTS.—Although it has been reported that in some patients as much as 150 grains (10 Gm.) of diuretin can be given without any untoward result, such large doses will not infrequently induce headache, nausea and vomiting. Diarrhea is the most frequent unpleasant accompaniment of the more moderate doses, up to 90 grains (6 Gm.) in the twenty-four hours. Other effects which have been witnessed are vertigo and tinnitus aurium, and in occasional cases evidences of central nervous excitation, such as restlessness, insomnia, tremor, and a peculiar feeling of fear. Most adults, however, bear 75 grains (5 Gm.) in a day well, and Hoffmann even found that debilitated patients could usually take up to 105 grains (7 Gm.) without disturbance. Krehl states, however, that after such large amounts a collapse-like condition has been observed, and advises that 75 grains be not exceeded.

Pawinski refers to the fact that diuretin may cause headache and tinnitus aurium "like after salicylic acid preparations." It is not unreasonable to suppose that, with the large doses often given, these symptoms are actually due to the salicylic constituent of diuretin. Where they are so marked as to interfere with the use of the drug, the substitution for diuretin of theobromine sodioacetate (see Agurin) would seem advisable.

In animals Schroeder found the fatal dose of theobromine to be five or six times higher than with caffeine. Frankly toxic doses of diuretin are said to produce vomiting, diarrhea, free salivation, dyspnea, elevation of temperature, cardiac acceleration, and diminished arterial pressure.

THERAPEUTICS.—Theobromine sodiosalicylate is useful particularly in **dropsy** due to cardiac or renal conditions. In nephritis most clinicians recognize that it can be employed without danger of irritating the kidneys. Among cases of renal disease the best results are seen in **acute nephritis.** Advanced **chronic nephritis** is not infrequently refractory to its action, though Klemperer states that in cases of moderate severity daily doses of 60 to 90 grains (4 to 6 Gm.) will increase the amount of urine 1 to 2 liters. In **parenchymatous** forms of **nephritis,** a number of observers credit the drug with the property of diminishing the albuminuria, at least temporarily. In the initial stages of **uremia,** good results from it have been reported.

> Report of experiments in which **acute nephritis** was produced with uranium nitrate in 82 rabbits and in about half of these diuretin given in amounts varying from large doses to doses equivalent to a 1-Gm. (15 grains) dose in the human subject. The results supported the view that in severe acute nephritis a diuretic drug such as diuretin is contraindicated, as in the experiments the drug somewhat shortened the period of survival of the animals. On the other hand, of the animals permanently surviving three-fourths had received diuretin. This rather gives support to the view that in less severe cases diuretin may be beneficial and so justifies the cautions use of the drug in moderately severe cases of acute nephritis. H. A. Christian and I. P. O'Hare (Arch. of Int. Med., May, 1913).

In **cardiac disease** diuretin is useful for several purposes. It is not only helpful as a diuretic in **valvular disease** with edema, in which condition it may frequently be combined with digitalis with advantage, but is sometimes useful as a substitute for drugs of the digitalis group when these prove ineffective in pronounced **chronic myocarditis**, the theobromine in it in this case exerting an action similar to that of caffeine—though less pronounced and constant, according to Sonnenkalb. The heart beats are strengthened and sometimes slowed.

> A patient advanced in years, suffering from arteriosclerosis and diabetes, had survived more than a hundred attacks of severe **pulmonary edema.** Fifteen grains (1 Gm.) of diuretin, given during an attack, always improved the heart action. Rosenfeld (Allgem. med. Zentralzeit., No. 18, 1909).

Theobromine is believed to dilate the coronary vessels—unless so sclerosed as to be rigid—much more than caffeine. This doubtless accounts for the excellent results reported from its use in moderate doses in **angina pectoris.** According to Pauli and Kaufmann, it sometimes acts so promptly in this condition that the attacks are checked almost at once. In some instances the patient remains free from the paroxysms when the drug, after a period of continuous use, is left off; in other cases it must be given again after a short rest.

The following combination of the drug with sodium iodide may be administered in anginal states:—

℞ *Theobrominæ sodio-*
salicylatis .... fʒj (4 Gm.).
Sodii iodidi .... gr. viij (0.5 Gm.).
Aquæ menthæ piper-
itæ,
Aquæ destillatæ....āā f℥iij (90 c.c.).

M. Sig.: To be taken at intervals in one day.

In marked types of angina, viz., those in which the pain is wholly projected to the back, shoulders, arms, lower jaw, etc., the drug has proven of the same utility as in angina pectoris. A number of clinicians have also praised its prompt action in the so-called **"angina abdominis"** or **arteriosclerotic colic,** ostensibly due to temporary spasm of already partially sclerosed mesenteric vessels. It is considered by Breuer to reduce the abnormal irritability of these blood-channels. According to Burwinkel, the diagnosis of abdominal angina can be made in cases of obscure abdominal pain through the rapid relief afforded by theobromine compounds.

As prophylactic against the **anginal attacks** seen with lesions of the coronary arteries, as well as those met with in **chronic tobacco poisoning** and **neurasthenia,** theobromine is usually more effective than the iodine preparations. Theobromine sodiosalicylate should be given in doses of 7½ to 9 grains (0.5 to 0.6 Gm.) three times a day; larger amounts are unnecessary and are, perhaps, less effective. Theobromine and allied compounds possess a definite vasodilator influence on certain vascular areas. This can be easily demonstrated in the case of the kidney, and the small vessels of the heart are probably affected in the same way. This results in diminished resistance and improved circulation, which accounts for the good effect in stenocardia. Improvement sets in after two or three days, and is often so marked that the results must be classed among the most striking which drug therapy can achieve. The treatment should be continued for at least two or three weeks, and the drug may be prescribed longer if it seems necessary. These small amounts are well borne by the stomach, and the author has never witnessed any harmful effects from long-continued administration of the drug. Von Noorden (Med. Klinik, No. 1, 1908).

In **arteriosclerosis** in general, the drug seems to prove useful in the hands of some observers. It has been especially recommended in the **headache of arteriosclerotics;** here doubtless the salicylate component is sometimes responsible for the results noted. As already intimated, theobromine tends to overcome undue excitability of the vascular tree, thus preventing it from going into spasm or overcoming the spasm where it exists. This would seem to account for the benefit noted by Kaufmann in **intermittent claudication.** It applies both to vascular nueroses without organic lesion and to arteriosclerosis in its earlier stages. Loeb refers to a useful effect of diuretin in cases of arteriosclerosis where the heart gives out owing to increased demands made upon it and because the thickened coronary vessels do not supply it with sufficient blood.

To obtain an effect with theobromine sodiosalicylate in **arteriosclerosis,** the major portion of the drug should be given during half a day, preferably in the afternoon. Small doses should be used—8 grains (0.5 Gm.) three to four times a day, increased to not more than 15 grains (1 Gm.) four times a day. Large doses can only be given for a few days in succession and with occasional days of rest after continuous use. The smaller doses—8 grains three or four times daily—may be given for a long time. Romberg (Deutsche med. Woch., No. 35, 1905).

According to Van den Velden and others, theobromine sodiosalicylate will effectually remove the bronchial spasm in cases of **asthma,** relieving the distress entirely or nearly so within fifteen minutes if the drug be ingested at the beginning of the attack. The dose to be used is 15 grains (1 Gm.) in water, which is repeated once, or rarely twice, if there is no relief after ten or fifteen minutes. The drug does not seem to lose its effect, even after daily use for some weeks.

In many cases of **asthma,** not alone of those of cardiac origin, but also those of the bronchial type, theobromine sodium salicylate gives good results. Often it is sufficient to give 15 to 30 grains (1 to 2 Gm.) of the drug before a paroxysm is expected, *i.e.,* as a rule in the evening. An advantage of the drug is that it can be taken for weeks without harmful effects. In the purely nervous forms of asthma the effect is inconstant. It is more certain in the bronchitic type of case, especially if heart weakness is simultaneously present. That the antidyspneic effect of diuretin has taken so long to become recognized is due partly to the name given it, which indicates only one of its uses, and partly to the fact that the dose employed has been too small. Meyer and Cahn (Deut. med. Woch., Sept. 19, 1912). S.

DORMIOL is a condensation product of chloral and amylene hydrate [$CCl_3.$-$CHOH.O(CH_3)_2C_2H_5$]. It is a colorless, oily liquid, having a camphoraceous odor and a peculiar, not unpleasant pungent taste. It is closely related to chloral hydrate, but less likely to produce toxic symptoms. The drug is not official.

PREPARATIONS AND DOSE.—A 10 per cent. solution of dormiol should be used, of which ½ to 2 fluidrams (2 to 8 c.c.) may be given. The commercial 50 per cent. solution may also be administered in capsules.

PHYSIOLOGICAL ACTION.—Dormiol is a reliable and safe sedative and hypnotic, but is not so powerful in its action as chloral hydrate.

THERAPEUTICS.—In simple **insomnia** of which pain is not the cause, dormiol may be useful. Small doses are sometimes of value in **convulsions** and **colic in infants.** Persistent **hiccough** may be relieved by the use of this drug. Dormiol has also been used to advantage in **chorea** and **paralysis agitans,** and may be employed in place of chloral hydrate in **delirium tremens.** H.

DROWNING.—In most cases individuals who have been asphyxiated from submersion in water for over five minutes are dead when they are taken out, but modern research has shown that the vital spark lingers long in the body cells and all efforts to revive the victim should be made, long after the five minutes have elapsed. Cases have been revived after immersion had considerably exceeded the usual limit, some as much as one-half hour.

Two cases of individuals who had been in the water for a time considerably longer than is usually followed by recovery. They tended to show that the best method of artificial respiration without apparatus is that of **Silvester,** where there is but one operator, and the combined **Sylvester and Howard methods,** as suggested by A. H. Smith, where there are two or more to assist in the work. These are the methods prescribed in the regulations of the Life-saving Service. The two cases reported and others cited from the literature urge the practice of persistence in artificial respiration for a period of at least two hours in all cases of the apparently drowned before hope is abandoned, especially where the known submersion has been for less than thirty minutes or where the time is in doubt. In the first case the man must have been more or less under water for at least *twenty-three minutes,* and some who witnessed the accident stated it to have been over half an hour, and it is very safe to say that his resuscitation was due entirely to the persistence and perseverance of the life-saving crew, who kept up the artificial respiration for over an hour and three-quarters, and thus supplied the energy for breathing until his blood and tissues had received enough oxygen to continue the process for themselves.

The second case had been in the water for nearly *half an hour,* and yet the boy recovered after somewhat over an hour of artificial respiration. Trask (Military Surgeon, May, 1907).

In a case reported by the writer, although ending fatally, the heart continued to beat a long time while artificial respiration was being given, illustrating the fact that efforts at resuscitation should be used for at least two hours. Failure to resuscitate this patient was due principally to irreparable damage having been done to the respiratory centers in the medulla by anemia. Hitchings (Jour. Amer. Med. Assoc., Nov. 23, 1912).

The first thing to be done is to promote the expulsion of the water from the respiratory passages. The best way to do this is to hold the patient in the vertical position the head downward. This is especially applicable in the case of children, but sometimes difficult when the patient is an adult. Laying the patient abdomen down over a barrel will sometimes act as a substitute. The next thing to do is to perform artificial respiration, of which there are several methods.

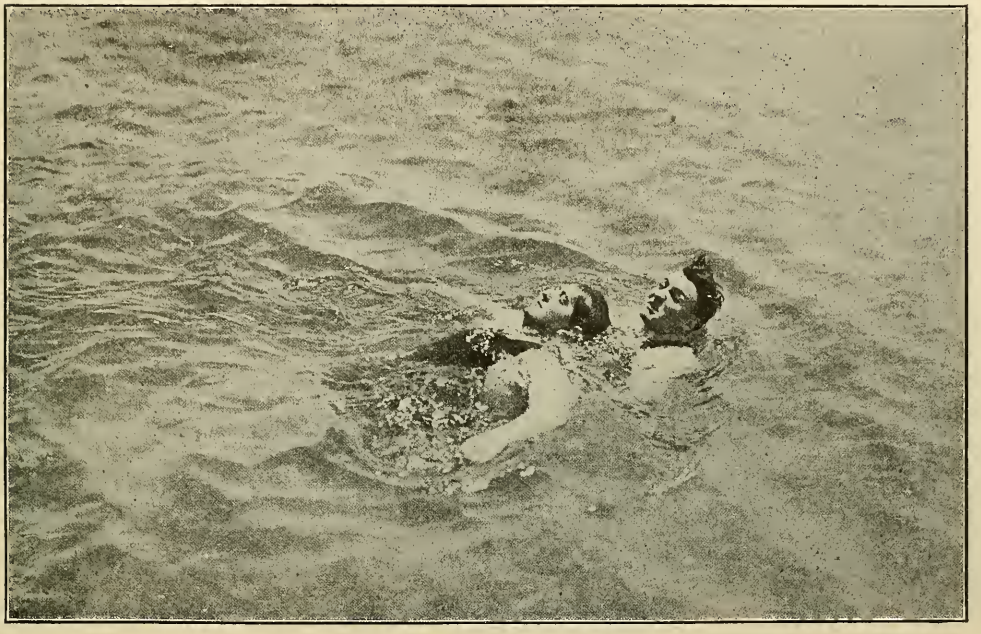

Fig. 1.—Grasping the body for rescue.

Apart from sequelæ, death from drowning appears to be due to asphyxia from the mechanical action of the water entering and blocking the air-passages; or shock from sudden and prolonged immersion. These may be combined, but in most cases one or other is the prominent symptom. If any considerable quantity of water has entered the bronchial tubes, unless it is very quickly expelled by a voluntary effort, such cases are hopeless. The condition is shown by the continued expulsion of froth when artificial respiration is performed, although the mouth and pharynx have been well wiped out before commencing. Barnes (Lancet, June 18, 1910).

Artificial Respiration.—Marshall Hall Method.—The folowing method was first described by Marshall Hall in 1857: The patient is alternately rolled from the lateral to the prone position, pressure being made on the back between the shoulder-blades while in the prone position. The advantage of this method is that the tongue does not fall back, obstructing the flow of mucus and water from the mouth.

Silvester Method.—Silvester described another method in 1858, but one disadvantage is that at least three persons are required to perform it. The patient is placed upon his back with a small roll under the neck, the shoulders being slightly raised. The arms of the patient are grasped just above the elbows by the operator, and gently moved away from the body to a point over the head. The ribs are thus raised and the capacity of the chest increased.

The arms are then brought down to the side, the elbows flexed and pressed against the chest. This decreases the capacity of the chest and expels the air from the lungs.

With the exception of the **Brosch-Sylvester method,** the **Schäfer method** of artificial respiration gives the greatest respiratory exchange for each thoracic movement. In addition to this, the tongue automatically falls forward, there is free drainage for the lungs, and long-continued application can be easily made, conditions which make it the best method for use in drowning accidents. Hitchings (Jour. Amer. Med. Assoc., Nov. 23, 1912).

Howard Method.—Still another method was described by B. Howard, of New York, in 1868. The operator kneels over the patient and exerts pressure on the lower part of the chest, diminishing the chest capacity. The pressure is then relieved, thus increasing the chest capacity. But in this method the tongue tends to fall back into the pharynx; the ribs may be fractured, especially in senile subjects, when they are quite brittle, and the liver is liable to be ruptured, as it is enlarged and congested in such cases.

Schäfer Method.—The "prone pressure" method seems to be the best so far described, and has the following advantages: It is fully efficient; can be easily learned; only requires one person to perform it, causing no fatigue, and it allows the tongue to fall forward. It was first described in 1890 by E. A. Schäfer, of Edinburgh.

In cases of drowning the prone pressure method of artificial respiration is always indicated. Its advantages are: (1) that it is fully efficient; (2) that it can be performed without fatigue by a single individual; (3) that it is simple and easily learned, and (4) that it allows the tongue to fall forward and the mucus and water to escape from the mouth, so that the tendency of these to block the passage of air, which is inherent to the supine position, is altogether obviated. It can be applied equally well in attempting to revive a patient whose respiration has ceased in consequence of an overdose of chloroform or other anesthetic. Schäfer (Jour. Amer. Med. Assoc., Sept. 5, 1908).

The patient is placed in the prone position, vertical pressure being applied over the ribs, the operator kneeling beside the

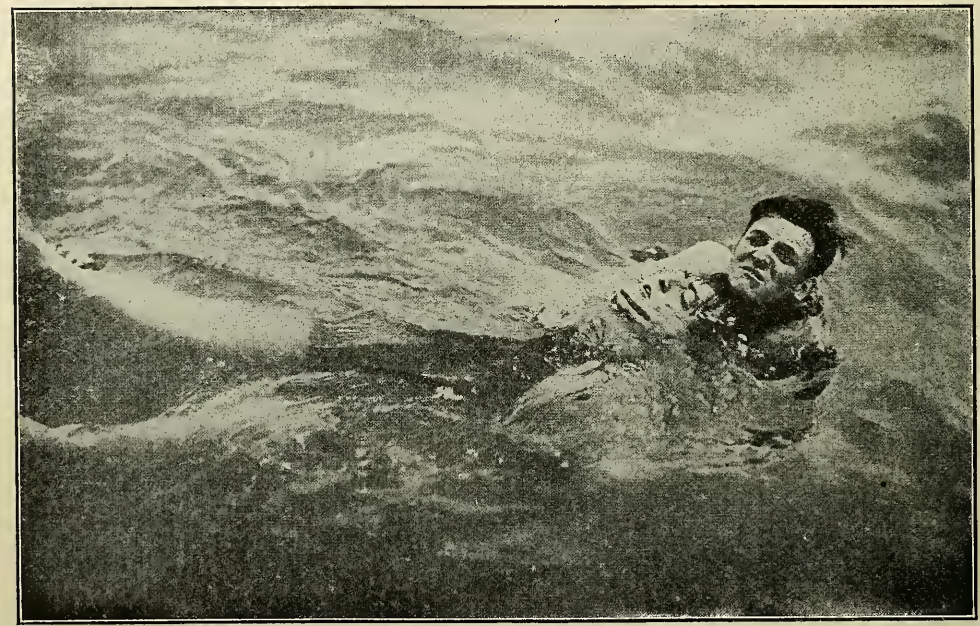

Fig. 2.—Position for rescue.

patient. This causes the thorax and abdomen to be compressed against the ground, the pressure on the latter forcing the viscera upward against the diaphragm, which moves upward, forcing the air from the lungs. The pressure is then relaxed and the parts return to their normal position, thus drawing the air into the lungs. This procedure is performed about twelve times a minute.

The **patient** should be **kept** as **warm** as possible, woolen blankets being wrapped around him after he has been thoroughly dried. During the artificial respiration **gentle friction** should be made always toward the center of the body. Artificial respiration should be continued as long as the heart continues to beat, and it is said the movements should be continued for from one to two hours after the heart has ceased to beat.

The usual directions given for the treatment of the apparently drowned are to perform artificial respiration and apply warmth. If, however, we look upon such as cases chiefly of shock, it is obvious that something more than this may be done. Shock may be looked upon as the result of a number of afferent impulses partially paralyzing the vasomotor center, and so causing a rapid fall in blood-pressure; the result of this is that the greater portion of the blood of the body stagnates in the splanchnic area, and the brain, including the circulatory and respiratory centers, is robbed of its proper supply, and these centers are still further depressed. The result to be aimed at, therefore, is the driving of the blood from the abdomen, so that the brain may receive its proper supply. This may be done by an attempt at **autotransfusion** as follows: Having started an assistant on artificial respiration, the author firmly bandages the legs from the feet upward. A roller towel is then passed round the patient's abdomen, the two ends crossing in front. One assistant is told off to each of these ends. As the arms are brought down to the chest in the *expiratory* movement of artificial expiration (Silvester's method) these two assistants, grasping the towel ends firmly with their right hands, pull them, at the same

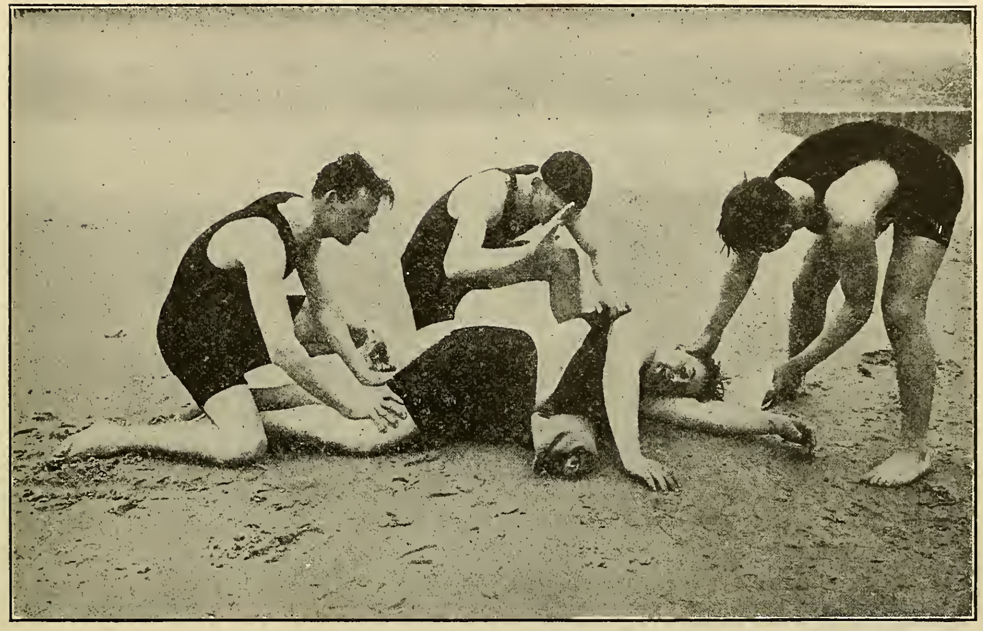

Fig. 3,—Stimulating respiration by slapping and massage.

time making pressure on the abdomen with their left hands. In this way considerable squeezing of the abdomen is obtained. As the *inspiratory* movement commences the pressure is relaxed so as not to interfere with the expansion of the lungs. The process is continued synchronously with the movements of artificial respiration. The idea is that this acts beneficially in two ways: (1) it assists, by pressing on the diaphragm, to more completely empty the chest with expiration; (2) it squeezes some of the excess of blood from the abdominal cavity. The bandaging of the legs and arrangement of the towel can be very quickly carried out with assistance, of which there is usually no lack in these cases. Gravity should also be made to assist the flow of blood to the brain by keeping the head at a lower level than the body. The writer gives a hypodermic injection of **ether** (30 minims—1.8 c.c.) and usually one of **strychnine** as well. The objection to the use of these stimulants—that they stimulate an already tired center and are quickly followed by increased depression—seems hardly to apply in cases of drowning, as when once reaction has set in recovery is usually rapid. **Adrenalin chloride** given hypodermically (30 minims—1.8 c.c. of a 1 : 1000 solution) should act beneficially by raising the blood-pressure. Barnes (Lancet, June 18, 1910).

The patient, reviving, should be removed to a warm room and kept quiet, and later such stimulation and tonics should be given as is deemed necessary.

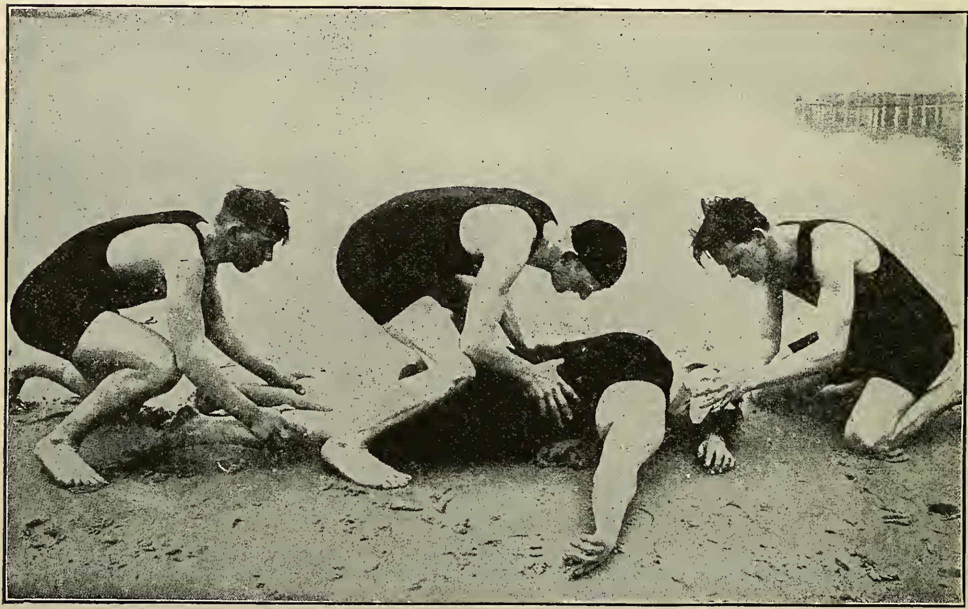

Fig. 4.—Expelling water from lungs and stomach.

In some cases of drowning attributed to cardiac failure the swimmer simply loses consciousness from cerebral anemia—*i.e.*, he faints, goes under, and inevitably perishes unless help is at hand. Apart from disease, such as aortic disease or cardiac dilatation, several other causes may bring about such a state of things. Among them are severe and prolonged muscular effort prior to swimming, and flatulent dyspepsia. Every person in the habit of swimming in deep water should have a medical examination from time to time. To enter the water with a full stomach is probably as dangerous as with an empty one. About two hours after breakfast or lunch is the best time. When the intestines have been emptied by a purgative and the circulation depleted thereby, swimming in cold water should be avoided. Lawrie (Brit. Med. Jour., Sept. 16, 1905).

The following details on the prevention of drowning, rescuing, and the treatment of the apparently drowned, published in the Pennsylvania Health Bulletin of May 12, 1912, under the auspices of Dr. Samuel G. Dixon, the Commissioner of Health, are so helpful that we take the liberty of presenting them practically *in toto*:—

"**Prevention.**—When in danger of being drowned the individual should remember that in order to keep afloat the hands and arms should be kept under the water and in motion; when they are held out of the water, the head is almost immediately submerged. It is not at all difficult to keep afloat, if this rule is followed, as the human body is of nearly the same specific gravity as water. If one can keep his presence of mind a very slight up and down motion of the hands and feet, paddling as a dog swims, will be sufficient to keep the head above water, and can be kept up for a long time without tiring. If unable to keep the head above the surface constantly, every time it goes under the mouth should be closed and the breath held, thus preventing strangulation.

"Prevention of chilling the body is of the greatest importance, and if there is long-continued exposure in the water as in the case of ship-wrecks, it is advisable to put on an abundance of woolen clothing, if at all possible.

"In salt water when the current sets out from land, as when the tide is going out, it is a mistake to struggle to reach the land. One should throw himself upon his back, whether alone or encumbered, and await help from the shore. Many persons perish by exhausting themselves in vain attempts at swimming, especially against the current, when it would have been safe to float with the face up, and to wait until rescued.

"**Rescuing.**—If there is no one present who can swim when an individual is drowning, a plank or any piece of wood or rope should be thrown to him to which to cling, urging him to keep his hands under water and to keep both hands and feet in motion.

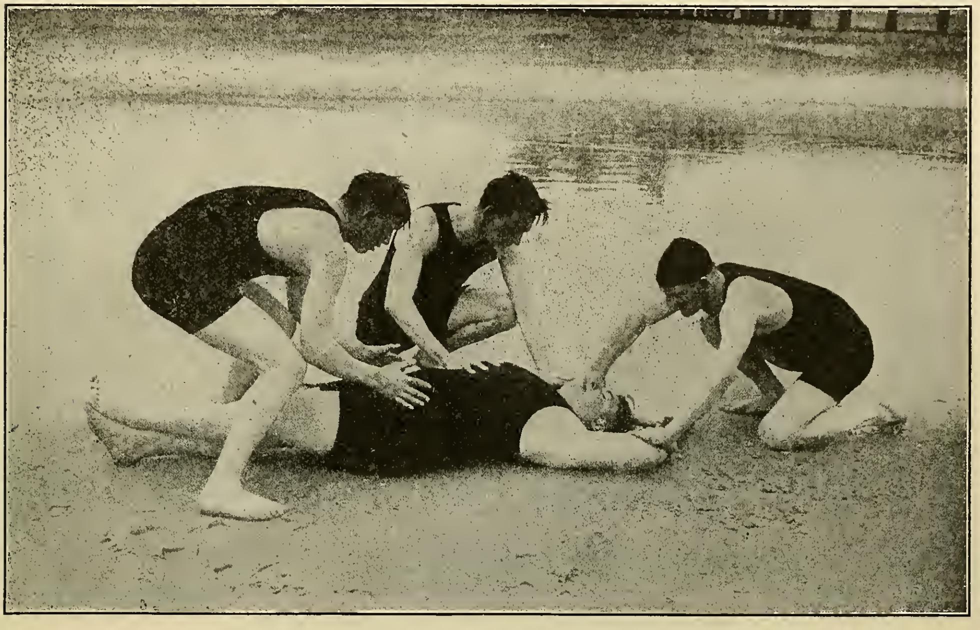

Fig. 5.—Inducing inspiration (more than one operator). Tongue held by handkerchief.

"Before swimming to the rescue of a drowning person, one should relieve himself of as much clothing as can be quickly thrown off. Be sure to loosen the legs of drawers if they are tied at the ankle. If this is not done, the garment is likely to fill and to act as a drag.

"Do not touch the drowning person so long as he still struggles. Wait until he becomes quiet, otherwise he may grapple with you and render you helpless. As you approach the drowning person, assure him in a firm voice that he is in no danger if he will keep quiet. Catch him quickly by the hair or collar, or under the arms, turn him on his back and give him a quick pull. (*Fig. 1.*)

"This last movement will bring him well up on the surface of the water for a moment. Now quickly throw yourself on your back and haul his back up to cover your stomach; the back of his head will then be on your chest; with both hands holding him, one placed on each side of the lower jaw, swim for your destination. (*Fig. 2.*)

"If one is a good swimmer he will get to safety in this way sooner than any other. Moreover, one will be able to keep his own face, as well as the face of the person who is being saved, above water. By maintaining the position described—the rescuer on his back and the rescued lying face up on the rescuer's stomach—one also will find that it is possible to float for quite a long time.

"If the person sinks before being reached, watch for the bubbles rising from the lungs, which will often enable you to locate the body. In flowing water allowance must be made for the direction and rapidity of the current, as it will carry the bubbles down stream from the body. In diving after a body you should seize it with one hand only, leaving the other free to be used in rising to the surface.

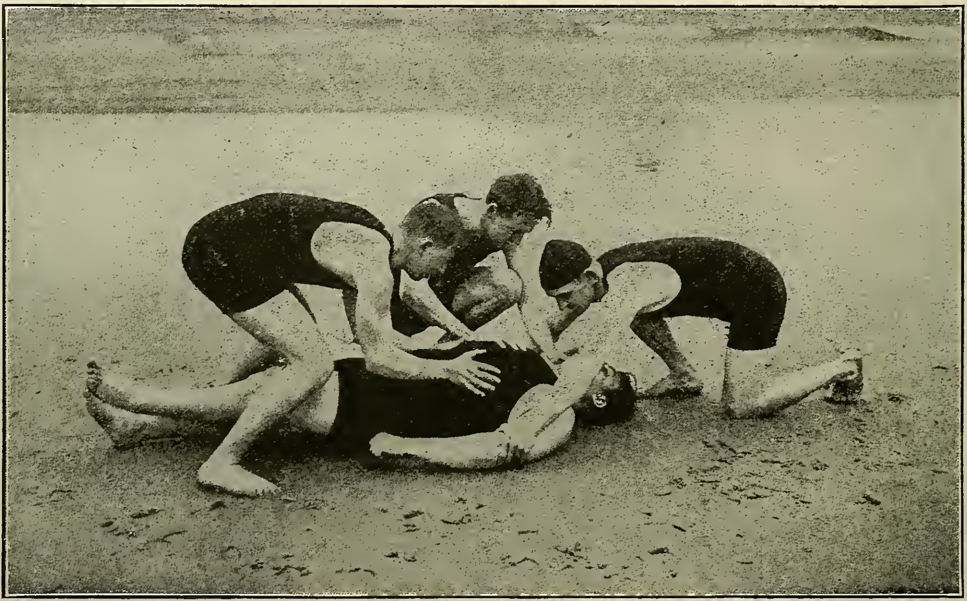

Fig. 6.—Inducing expiration (more than one operator).

"**First Treatment of the Apparently Drowned.**—The first impulse in discovering the body of a drowned person is to summon a physician. Unfortunately, however, under circumstances attending this accident the physician is so infrequently present or within reach that the most valuable time is lost in searching for one. Upon discovering a body every effort should be made at once to resuscitate the victim. It is of the utmost importance that everyone should understand the few simple measures necessary to retain life; and, as it may be necessary to maintain efforts for a long time, it is important that all methods should involve as slight an outlay of the rescuer's strength as possible. In each instance the aim should be to restore breathing. If the heart has ceased to beat the person is probably dead, but the time required to determine whether this is the case may be fatal. Efforts to restore respiration should be begun at once. Very efficient methods for the restoration of respiration by various mechanical devices are in use by large industrial corporations and by many institutions, and are of service when one is apparently dead from electrical shock or from inhalations of water, gas, smoke, or poisonous vapors. The following method, if carefully carried out, will give maximum results:—

"**Rule I. Preliminary Treatment.**—Do not move the patient far from the scene of accident unless he is in danger of freezing. Do your best to keep people from crowding around and shutting off the air. Wipe dry the mouth and nostrils, quickly open the clothing sufficiently to expose the chest and waist. Turn him upon his face, placing one forearm or some other prop under the forehead to keep the nose and mouth free from the ground, keeping the face turned down and heading to the wind, as you want all the movement of air possible. Place a roll of blanket or clothing under the upper portion of the abdomen just below the tip of the breast-bone, as shown in *Figure 3*. Turn his body on its side for a moment and slap the bared chest smartly two or three times with the open hand and let him fall into his former position. (*Fig. 3.*)

"If the patient does not immediately begin to revive, proceed according to Rule II.

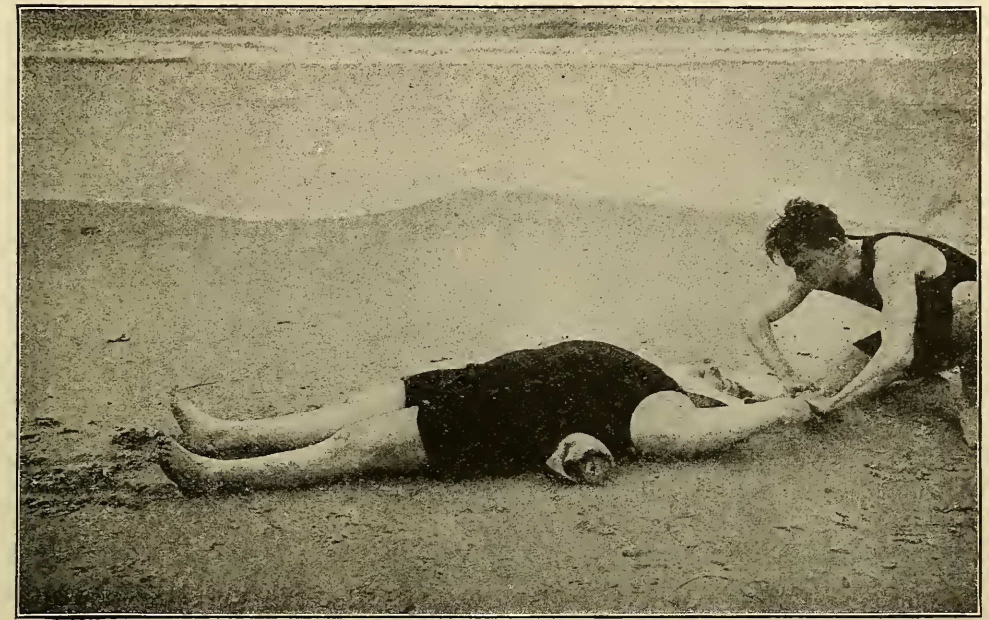
Fig. 7.—Inducing inspiration (one operator). Tongue held between the teeth.

"**Rule II. To Expel Water from the Body**—Separate the jaws and keep them apart by inserting something hard between the teeth—a piece of wood, rock, or cork, anything to keep the mouth open. (*Fig. 4.*)

"Take position astride the patient's hips with your elbows resting upon your own knees, and your hands over the body ready for action. Make pressure on the base of the chest until the flow of water from the lungs is slackened. Relax and again make pressure, alternating relaxation and pressure until the lungs are empty. This procedure should not last longer than thirty or forty seconds and permits the entrance of sufficient air to stimulate respiration.

"Rule III. To Produce Breathing.—Clear the mouth and throat of mucus by means of a handkerchief, piece of garment or any rag wrapped around the forefinger. If ammonia, bay-rum, or ether is at hand, use the fumes to stimulate respiration by holding the bottle in front of the nose. Turn the patient upon his back with the roll so placed under him as to elevate the stomach above the rest of the body. Let an assistant, using a handkerchief, draw the tongue out at the corner of the mouth and keep it projecting between the lips (this prevents the tongue dropping back and closing the windpipe). Now let another assistant, placing himself above the patient's head, grasp the patient's arms just below the elbows and draw them steadily upward and over until they extend past the head, parallel with the ground, the hands meeting, as in *Figure 5.*

"(This movement expands the chest and induces inspiration.) The person at the head now moves the patient's arms down beside the body as in *Figure 6.*

"The assistant who holds the tongue, changing hands if necessary, so as not to interfere with this movement. Just before the patient's arms reach the position last described, the man standing over the body will grasp it with both hands, letting the balls (base) of the thumbs rest on either side of the pit of the stomach, and allowing the fingers to fall into the depressions between the short ribs. Now using his knees as a pivot he will, at the moment the patient's hands touch the ground, throw (but not too suddenly) all his weight forward on his hands and at the same time squeeze the waist, increasing the pressure while he slowly *counts four,* and after a final push lets go. (A child or a delicate person should of course be handled more gently.) At the instant the pressure on the chest is released, the operator at the patient's head will again draw the arms upward and hold them extended beside the head while the *count of four* is repeated. This manipulation of the arms and chest is called the bellows movement. It should be kept up deliberately and perseveringly.

"If natural breathing be not restored within, say, four minutes it may be because the air-passages are obstructed by mucus

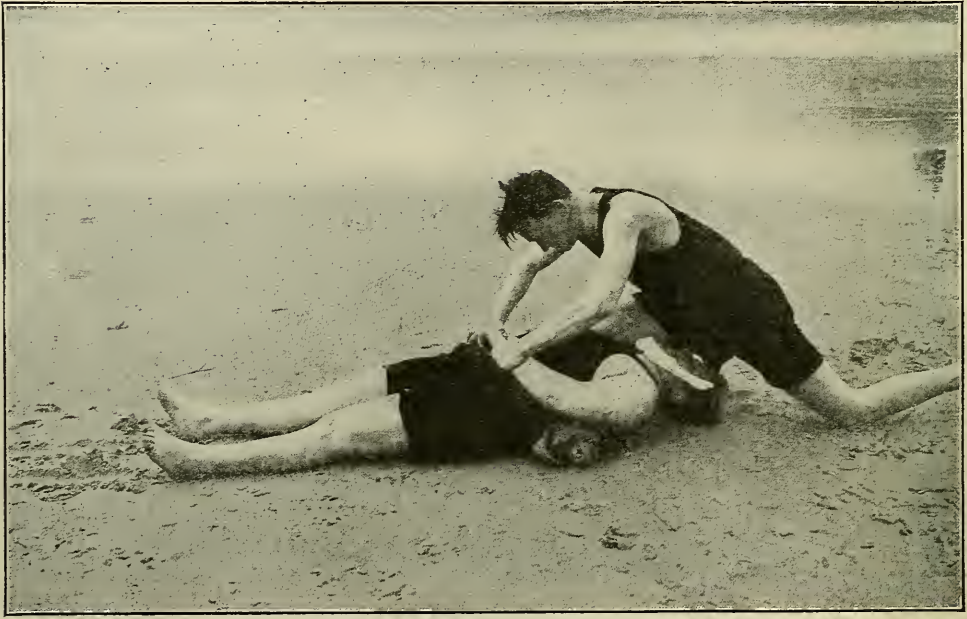

Fig. 8.—Inducing expiration (one operator).

or water. In any event turn the patient again upon his chest and do as directed in Rule II, rolling the body over in the opposite direction from that in which it was turned when the rule was first followed. After repeating the directions of the rule turn the patient once more upon his back and continue artificial respiration for from one to four hours, or until breathing is established or a physician has declared him dead.

"While care should be taken not to interfere with the action of those working the bellows movement, the limbs of the patient should be rubbed from the very beginning if a sufficient number of persons are at hand. The rubbing should be done *always toward* the body with a firm grasping pressure, using the bare hands, dry flannels, or handkerchiefs. If possible, warmth of the body should be promoted by the application of heated flannels to the stomach, and hot-water bags or heated bricks or stones to the limbs and soles of the feet.

"**When No Assistants are at Hand.**—If one person must work alone, first, do as directed in Rules I and II, then place the patient face up, as in *Figure 7*.

"With rolled blanket or clothing under his back, take position above the patient's head; grasp arms near the wrists and draw them steadily upward and forward (movement to induce inspiration) as instructed in Rule III. Next lower them (here the operation differs from that employed when two persons are working the bellows movement) to the patient's sides, bend them and bring them toward each other until the hands meet over the lower ribs, then press downward and inward with a firm, steady pushing movement, as in *Figure 8*.

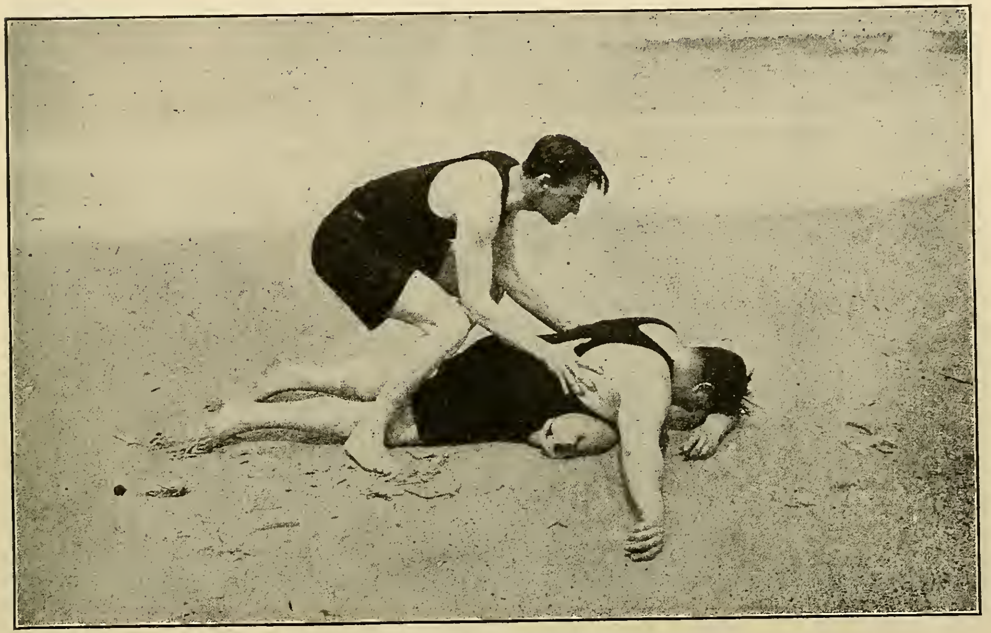

Fig. 9.—Inducing inspiration by relaxation of pressure.

"Repeat these movements while counting as directed in Rule III. If the jaws be separated the teeth may be made to hold the tongue at the corner of the mouth by passing a handkerchief under the chin and tying it over the head.

"**Alternate Method.**—If the patient has been in the water for a long period of time or, if for any reason the work of resuscitation depends upon only one person, the following method can be used and can be kept up for a longer time without great exhaustion.

"The patient is placed on his abdomen in the position shown in *Figure 3*. The operator kneels across the patient as in *Figure 9,* the hands being placed at the base of the chest over the lowermost ribs in such a way that the extended fingers are about six inches below the armpits. (*Fig. 9.*)

"Now swing your body forward so as to have your weight fall at a slight angle on the wrists; the elbows are braced against the knees so that the weight of the body is augmented by such pressure as may be had by forward pressure of the feet and legs; the legs act as the fulcrum. (*Fig. 10.*)

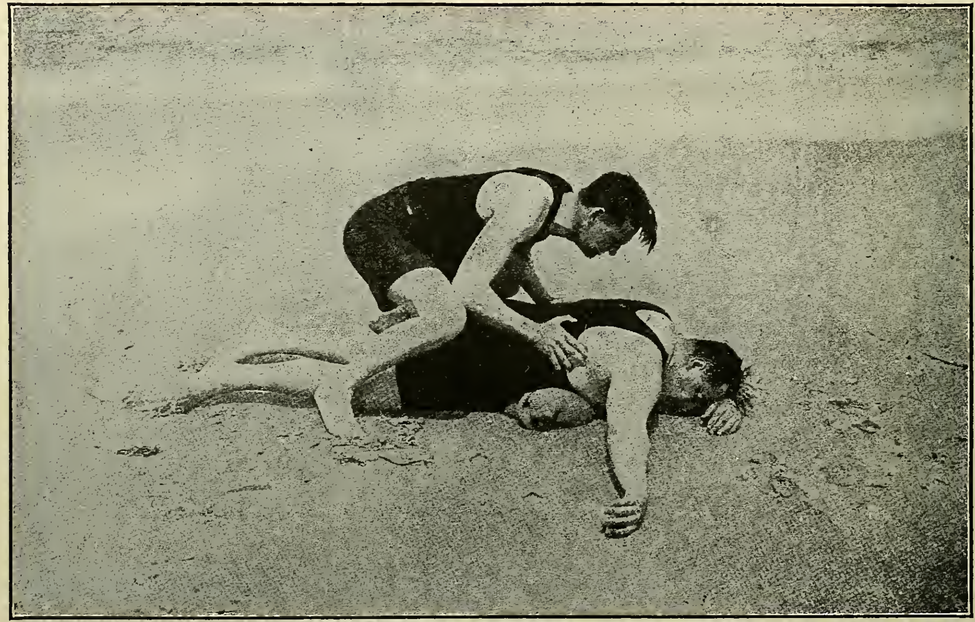

Fig. 10.—Producing expiration by direct pressure.

"This makes lateral and slightly upward pressure on the base of the chest and expels the air from the lungs. Swing back, releasing the pressure as shown in *Figure 9,* and the lungs fill by normal expansion.

"Repeat this motion slowly, about 12 times per minute, exerting no more force than is necessary to cause a deep expiration. The latter can be estimated by the sound made by the air escaping from the mouth and nostrils. (Be careful not to make too deep, sudden, or violent pressure, as injury may be done to the organs beneath.)

"When the patient is beginning to breathe, the process of artificial respiration should be stopped. Place the patient on his back and press the base of the chest *every other* time he breathes *out,* as described under Rule III, *Figure 6.* This should be continued until he can breathe naturally (not too rapidly) without assistance. As soon as this is accomplished the measures described as the "After Treatment" should be carried out.

"**Rule IV. After Treatment.**—As soon as breathing is established the patient should be stripped of all clothing, wrapped in blankets and put to bed comfortably warm, but with plenty of fresh air. Whisky, brandy, or other stimulants, and hot water, should be given in teaspoonful or dessertspoonful doses, at intervals of ten or fifteen minutes during the first hour.

"After reaction is fully established there is danger of congestion of the lungs, and if perfect rest is not maintained for at least forty-eight hours the patient may be seized with great difficulty in breathing. If this happens death is likely to occur unless immediate relief is afforded. In such cases a large mustard plaster should be applied to the chest. Should the patient begin to gasp before the plaster takes effect, carefully assist respiration by the bellows movement as explained in Rule III."

Accessory Measures.—Various accessory measures may be employed to assist resuscitation. Prominent among these is **adrenalin chloride,** 30 drops with saline solution (at 108° F.—42.2° C.) injected intravenously, or into the radial as recommended by Crile. The needle of the saline solution apparatus is the one introduced into the vessel, while the hypodermic syringe containing the adrenalin is plunged into the rubber tube of the apparatus, and the drug allowed to mix with saline solution drop by drop. When this measure cannot, for one reason or another, be carried out, intramuscular injections of 10 to 20 minims (0.6 to 1.2 c.c.) of **adrenalin** may be tried. **Bleeding** is advocated by some others particularly with the above measures carried on simultaneously.

The **Laborde method,** which consists in drawing out the tongue, held with a handkerchief to prevent slipping, rhythmically eighteen times a minute, is very helpful, assisting greatly artificial respiration. **Oxygen,** ready to be inhaled as respiration is resumed, greatly hastens recovery.

The **induced current,** one pole being applied over the phrenic nerve and the other over the sixth costal interspace, on either side, the sponge being moistened in salt water to insure penetration, sometimes causes violent contractions of the diaphragm, which also aids the artificial respiration method carried on simultaneously.

When nothing seems to cause the heart to resume its beats, **pricking of the heart** with a sterilized or carefully washed shawl-pin, through the chest wall, will sometimes suddenly cause it to resume its beats. As a last resort, opening of the abdomen to practise **heart massage** (see page 138 in the third volume) might be tried.

All methods indicated in the treatment of shock (*q.v.,*) or asphyxiation by gases are as applicable to the treatment of drowning.

H. AND S.

DUBINI'S DISEASE. See CHOREA.

DUBOISINE is the poisonous alkaloid of the leaves of *Duboisia myoporoides,* a plant growing in Australia. It crystallizes in fine, colorless needles, and is considered practically identical with hyoscyamine. The drug is not official.

PREPARATIONS AND DOSE.—This alkaloid is generally used in the form of duboisine sulphate, the dose being 1/200 to 1/50 grain (0.0003 to 0.0013 Gm.).

PHYSIOLOGICAL ACTION.—Duboisine sulphate is used as a sedative, hypnotic, and mydriatic. It tends to disturb digestion, producing a disagreeable taste in the mouth, excessive dryness of the mucous membranes, and a loss of appetite. In those having an idiosyncrasy it may cause sweating and salivation. It is said to decrease the quantity of urine and to have a deleterious effect upon nutrition. It is rather irregular in its action.

THERAPEUTICS.—Duboisine sulphate may be used instead of atropine to produce mydriasis before ophthalmoscopic examinations, the after-effects being less persistent than when atropine is used. It is recommended in the **night-sweats of phthisis** and **vesical tenesmus.** The drug may also be used for its sedative effect in great **mental excitement.** De Montyel found that large doses of duboisine produced vomiting in the insane without any evidence of nausea. In **epilepsy** and **paralysis agitans** the drug is sometimes useful, 1/100 grain (0.0006 Gm.) being given three times a day. It may be employed as a hypnotic in **insanity,** and is said to be less dangerous than hyoscine.

H.

DUOTAL. See GUAIACOL CARBONATE.

DYSENTERY, or Bloody Flux.

DEFINITION.—An intestinal flux of bacillary or amebic origin, occurring sporadically or in endemic or epidemic form. The large bowel (rarely the small intestine also) is the seat of an intense inflammation with ulceration, necrosis or gangrene, characterized clinically by frequent, serous, bloody stools, with more or less mucus, with tormina and tenesmus, and, in the acute phases, accompanied by fever.

VARIETIES.—Two definite types exist, etiologically considered, viz., *bacillary* and *amebic,* though *pseudo* forms may result from dietetic errors, mechanical or chemical irritants or ptomaine poisoning, rarely from parasites. True dysentery differs in its cause, course, severity, type of lesion, complications, mode of transmission, and geographical distribution. It is customary with some authors to speak of dysentery other than amebic, as catarrhal or diphtheritic or, more correctly, diphtherial; but it seems unwise to employ an incidental pathological lesion in a terminological sense when the actual causative factor is known. We shall consider it therefore from the etiological standpoint as bacillary and amebic.

BACILLARY DYSENTERY.

This may develop in any inhabited region of the globe, increasing in frequency and severity as the subtropical zones are approached. It occurs sporadically or in endemics or epidemics. Our knowledge concerning the common origin of these various forms, the *Bacillus dysenteriæ* varying only in certain minor details, we owe especially to the work of Flexner and his pupils, Vedder and Duval.

Sporadic dysentery speaks for the ubiquitousness of the causative organism as it may arise anywhere and at any season, especially in the senile, less frequently in children, and particularly in those whose nutritional state for any reason is depraved. Endemic dysentery is a disease of warm climates, where it may be met at any season, though of greater incidence during the periods of greatest heat, and more or less constantly in the tropics, where seasonal variations are less pronounced.

Epidemic Dysentery.—At long intervals this has occurred over great areas, arising in scattered foci, often remote from one another, subsiding during the colder periods to reappear with increasing violence during the summer, and perhaps reappearing over a period of several years. Local outbreaks are more common, however; indeed, they are the rule during hot, dry seasons in most of the countries of continental Europe. Epidemics also occur in such institutions as jails or asylums, homes for children or the aged, and in camps or barracks. These may occur at any season, but the two chief factors of collateral import are heat and drought. The hygienic and social status of people are likewise of determining importance.

> Bacillary dysentery is endemic in the Philippine Islands at all times, occasionally assuming epidemic proportions over more or less wide areas. The disease is due to at least three types of dysentery organisms, the well-known Shiga and Flexner types and the less-known organism of Morgan. Phalen and Kilbourne (Military Surgeon, April, 1910).

SYMPTOMS.—The incubation period, according to Strong and Musgrave, does not exceed forty-eight hours. The invasion is usually abrupt, occasionally preceded by constipation, usually ushered in with diarrhea, which in some instances does not in itself excite suspicion as to its real character. Fever, abdominal pain, and frequent stools are usually the first symptoms, with loss of appetite and malaise. At first mucous stools; then bloody, even pure blood, with distressing tormina and tenesmus, the pain being most intense about the umbilicus and radiating over the outer confines of the abdomen especially, accompanied by nausea, sweating, and more or less collapse. Any food or drink at once excites peristalsis. The desire to evacuate, at first temporarily relieved by a movement, becomes constant and increased by the act. In consequence of frequent, irritating stools, the anal region and rectum become intensely inflamed, at first with increased sphincter contraction, then relaxation and, still later, rectal prolapse. As in any case of severe diarrhea, there is a tendency toward vesical tenesmus also, probably due to the close autonomicocerebrospinal association of bowel and bladder. Frequent, burning micturition results. During the early stages, within the first few hours in fact, the appetite is more or less completely lost, the tongue is coated, and the patient complains of chilliness and fatigue. A moderate fever may exist. Occasionally the disease is ushered in with a rigor, though rarely. In the most acute cases the apogee may be reached in forty-eight to sixty hours, the sufferer having almost constant stools with great pain, thirst becomes intense, delirium supervenes, and death may occur from the third to the fifth day. In less severe types the course may extend over several weeks, the frequency of the stools gradually lessens, the pain abates, temperature falls to normal, though the patient may remain weak and anemic for some time. A mild icterus occurs in some individuals during the course of an attack. Vomiting is not a prominent feature in this condition. The urine is diminished in proportion to the severity of the malady, and a febrile albuminuria develops. Considerably more albumin is lost in the serous stools. In most cases lasting a number of days, the heart becomes rapid, the heart muscle becomes weak and irritable, so that a small, rapid pulse often occurs, and may persist for some time after convalescence is established. The most severe cases run a short course with a high mortality. The less acute forms may extend over a period of many weeks, emaciation progressing to a marked degree. In every epidemic, cases are met with in which the chief or even the only symptom is diarrhea, and but for their relation to other cases in the same locality, and the fact that the dysentery bacillus has been found in the stools of such individuals, their true nature would pass unrecognized. Sporadic cases of the same character are met with in temperate zones which run their course with little or no fever. Probably many of the diarrheas occurring in bottle-fed babies are of this character, as we now know that form to be which is most apt to occur during the summer months, and which is often called cholera infantum. Diphtheritic dysentery is merely one form of bacillary dysentery, in which the intensity of intestinal involvement is so great as to result in marked infiltration and necrosis of the mucosa. Apparently mild cases may quickly become grave by the development of gangrenous foci, or the case may have been of great intensity from its incipiency. These latter are spoken of as primary diphtheritic or gangrenous types, the former as secondary gangrenous or diphtheritic dysentery. Shreds and sloughs of the mucosa may be seen in the stools as well as pus and blood. Rarely a cast of the bowel may be passed. These cases, when well developed, belong to the most severe and fatal type, and though recovery may occur, it is not the rule; fall of temperature, collapse, dry tongue, coma—in short, the typhoid state precedes death.

The mortality statistics of epidemic dysentery are given by Vaillard and Dopter for the following countries: Japan, 24 per cent. (Shiga); Moscow, 12-17 per cent. (Rosenthal); Westphalia, 11 per cent. (Kruse); Toulon, 6-9 per cent.; Brittany, 20-50 per cent.; Finisterre, 50-60 per cent.; the difference in the severity of the disease being due, according to these authors, to differences in the virulence of the bacilli. Corney (Jour. London School of Trop. Med.; Austral. Med. Jour., June 15, 1912).

Chronic dysentery differs chiefly in the milder but more protracted course. The patient becomes weak, anemic, more or less emaciated, and presents an array of gastrointestinal disturbances in which diarrhea of the lienteric type is a prominent feature.

COMPLICATIONS AND SEQUELS.—A not infrequent complication is joint involvement. Some observers have dignified this condition by a special classification,—arthritic dysentery. This is not justifiable. The relationship was noted by Sydenham, who said "there was pain in the muscular parts of the body—especially at the joints—like the pain of rheumatism. Besides this, there was an inflammation of the fauces; like (but milder than) a quinsy." He noted, too, that this tendency was more marked in some epidemics and during some seasons than in others. This has been confirmed by modern observers. The large joints particularly are involved, but cardiac complications, *i.e.*, valvular involvement, play no part, though in any severe case of dysentery the heart muscle is affected to a variable degree. Other serous membranes may be attacked, however, pleurisy or pericarditis resulting. Peritonitis may occur without perforation, though, as a rule, it is due to separation of deep sloughs with consequent perforation. A periproctitis may be caused in the same manner. Thrombosis is a possible though not a common complication. Pyemic phenomena may arise, such as pylephlebitis, mycotic abscesses in other organs (as the spleen, for instance, which may spontaneously rupture), septic nephritis or parotitis, with chills and fever. Since malaria may be a concomitant infection in some cases, an examination of a fresh or stained blood-smear should be made. Apart from the multiple abscesses of a pylephlebitis, not a common complication, a single abscess of the liver is even less common in bacillary dysentery. In temperate climates there are no phenomena associated with an attack of this type of dysentery, which may be directly ascribed to the liver, enlargement of that organ and jaundice being so exceptional. In the tropics, however, the so-called "tropical liver" occurs so frequently that it is not surprising that the chronic congestion and enlargement become more pronounced in the course of an attack of dysentery. A heaviness in the right hypochondrium, with pain on pressure, and more or less jaundice are the rule. A rigor may bespeak the development of a liver abscess, but this latter often proceeds so insidiously as not to attract special attention.

Marcans identified hepatic abscess by the pain in the right shoulder, the leucocytosis with polynucleosis, and repeated X-ray examination. The first radioscopy was misleading. Repeated exploratory puncture was also useful. Zancarol was unable to discover the abscess in one case even with thirty punctures. In case of inversion of the viscera the diagnosis may be almost impossible, as in a case seen by Alvarez in which the patient was finally cured by resection of two ribs on the left side and evacuation of a large hepatic abscess. A. Chauffard (Bull. de l'Acad. de Méd., May 5, 1908).

Cases of dysenteric abscess of the liver in France which showed the same characteristics as the tropical abscess. It may follow a mild dysentery which may not have attracted attention, and it may run a latent course simulating a tuberculous process in the lungs, pneumonia, pleurisy or a suppurative hydatid cyst. In acute suppurative hepatitis with multiple abscesses, or an abscess with necrosis, the general symptoms may suggest typhoid fever or severe jaundice and the actual abscess be overlooked. The principal complications of these bacillary liver abscesses are adhesion between the focus or foci and the colon; perforation into the air-passages or pleura; pus collecting below the diaphragm, multiple abscesses in the left lobe of the liver, and postoperative bile fistula. Boinet (Bull. de l'Acad. de Méd., June 29, 1909).

In long-standing cases, where anemia has become marked, edema occurs, in part due to the blood change, and no doubt in part the consequence of a weak heart muscle. A rare complication of bacillary dysentery is multiple neuritis.

The sequelæ are not as common as one would expect from the nature of the disease. Many individuals never completely recover their health, especially after the more chronic forms of the disease, intractable dyspepsia and intestinal irritability remaining.

Of 71 cases of tuberculosis investigated 11 patients (15.5 per cent.) had a well-marked history of recent chronic dysentery. It is probable, that dysentery was a predisposing factor in a larger proportion of the fatal cases, because the fact of there having been repeated attacks of dysentery would not be noted in a necropsy report on a case of tuberculosis unless the connection was very strong or unless one were specially looking out for such cases. Gillitt (Indian Med. Gaz., Dec., 1910).

Cicatricial stenosis is rare. The symptoms are those of a slowly progressive and chronic obstruction of the bowel, swollen and tender abdomen, flatulency, paroxysms of intestinal colic, small and difficult stools, with increasing toxemia. Death may be due to obstruction or to some intercurrent malady. Prolapse of the rectum, hemorrhoids, proctitis, cystitis, chronic nephritis, anemia and edema may also be numbered among possible sequelæ. Relapses may occur during or even after convalescence, especially in those addicted to alcohol. Undue physical effort or the use of irritating food may invite reinfection.

Features of a relationship the writer has found to exist between a "crisis" or period of sudden improvement in cases of acute bacillary dysentery and the elimination of chlorides. Early in the disease there is oliguria. The elimination of urea is diminished in afebrile cases; that of chlorides is almost *nil* (0.2 Gm. in 1 instance), while that of phosphates is relatively but little decreased. In cases tending toward recovery there occurs a sudden increase in the urinary chlorides to above the normal amount, in addition to polyuria. While the salt lost through the alvine discharges early in the affection may be considerable, and the intake is low owing to dietary restrictions, these circumstances do not wholly account for the low chloride elimination. The author concludes, therefore, that there is a systemic retention of chlorides in this affection. Successive injections of 150 and 200 c.c. of salt solution in an adynamic case of dysentery were badly borne, inducing restlessness and dyspnea. L. E. Bertrand (Bull. de l'Acad. de Méd., Nov. 28, 1911).

DIAGNOSIS.—Bacteriological examination of the stools, while yielding definite results, is a difficult and time-consuming procedure. Agglutination of a known culture of the Shiga or Flexner-Harris type, by means of the patient's serum, is the most practical procedure. Both of these will react, the Shiga to a less extent than the Flexner-Harris, however.

The writers have made a systematic study of certain methods of diagnosis from the blood-serum in infants suffering from infectious diarrhea. Of 45 cases of infantile dysentery, dysentery bacilli were isolated in 38 cases (84.4 per cent.). In 35 of these bacteriologically positive cases mannite-fermenting strains only were isolated. The mannite-non-fermenting variety (Shiga) was isolated in 3 cases, in 1 of which it was found in conjunction with fermenting strains. Dysentery bacilli (acid mannite) were found in 1 of 15 control cases. Evidence of reaction on the part of each patient to either mannite-fermenting or mannite-non-fermenting types of dysentery bacilli was sought in the blood-serum. In every case, so far as practicable, three methods of serum diagnosis were employed, the well-known reactions of agglutination and of fixation, and one novel reaction, the reaction of conglutination. Lucas, Fitzgerald, and Schover (Jour. Amer. Med. Assoc., Feb. 5, 1910).

As in the case of typhoid fever, in which J. McCray showed that it takes six days for agglutinins to develop, so in bacillary dysentery, this test can only be used after the sixth or seventh day. In the epidemic, asylum or institution type, bacilliary dysentery is not difficult of recognition nowadays, and to these we are justified in adding the summer diarrheas of infants, especially occurring in the bottle-fed. The sporadic case, however, can only be suspected, more or less strongly, without laboratory diagnosis.

The writer studied 37 cases of asylum dysentery, and in practically all of those with blood or bloody mucus in the stools was found the Flexner type of the dysentery bacillus. In 44.4 per cent. of normal stools the writer found a dysentery-like organism, which differs from dysentery, colon, and typhoid bacilli; hence it may be classed with the so-called pseudodysentery group. Fisher (Jour. of Med. Research, May, 1907).

Instance of invagination of the intestine mistaken for dysentery. The child, aged 4, had diarrhea, melena, pain, and vomiting for three weeks; then peritonitis developed, fatal in a week. Treatment had been on the diagnosis of dysentery, with serotherapy, etc., but necropsy revealed invagination of the colon, although during life the palpation findings had been negative. J. Comby (Arch. de méd. des enfants, Jan., 1912).

Where gangrene of the intestinal mucosa supervenes, the peculiar odor, profound infection, and the passage of foul, necrotic sloughs or casts will serve to render diagnosis comparatively easy.

The diseases most often confounded with dysentery are carcinoma, polypi, and syphilis of the rectum; hemorrhoids and, in those returning from the tropics, bilharziasis. The following points should be remembered in the differentiation of the two forms: 1. Amebic dysentery, unless skillfully treated at the beginning, runs usually a chronic course, while the bacillary form lasts only from four to eight days in mild cases and from three to six weeks in serious ones. 2. In the amebic form no bacilli can be found except under the rare conditions of a mixed infection, with both amebæ and bacilli. 3. Toxic symptoms, such as high fever, rapid emaciation, and nerve complications, exist in bacillary dysentery, but not usually in the amebic form. 4. Liver abscess is a frequent complication of amebic dysentery, and does not exist in the unmixed bacillary form. The conditions necessary for a certain diagnosis of bacillary dysentery are the positive agglutination reactions of the dysentery bacillus with the blood-serum of the patient. Sandwith (Lancet, Dec. 7, 1907).

Case of dysentery due to the rare monad, *Balantidium coli.* The disease has been attributed particularly to the habitual consumption of fresh sausage, the parasite being commonly found in the intestine of the hog. Those who handle hogs or assist in the preparation of hog sausage, are liable to contagion. Of 74 cases published during the ten years 1891 to 1901, 26 of them, that is, 35 per cent., the connections of the patient in one way or another with hogs is clear. Another source of infection might be the drinking-water. It is reported to have been found in the water of the city of London. It preserves its motility for a long time in water at ordinary temperature; it stands cold better than most protozoa.

Diarrhea is the most frequent symptom of balantidium infection of the intestine, 99.1 per cent. of the reported cases. This diarrhea is tenacious, ceasing only when direct treatment is given. Another frequent symptom is intestinal colic; nausea and vomiting may occur. In some cases there is abdominal distention; frequently there is pain upon pressure over the colon. On palpation the colon feels thickened. Tenesmus is a common symptom. When the infection has lasted for some time, there is weakness, exhaustion, and emaciation; more or less intense anemia and at times edema of ankle and feet. Taboadela (Sanidad y Beneficiencia, Jan., 1911).

As to the clinical differential diagnosis of amebic and bacillary dysentery, Major R. J. Blackham (Jour. Royal Inst. of Public Health, Feb., 1908) offers the following comparative points:—

AMEBIC.

1. Always chronic in its course.
2. Pyrexia rare.
3. Ionic symptoms not present except when there is liver abscess.
4. Liver abscess occurs in about 16 per cent. of cases.
5. Small intestine frequently attacked.
6. Undermined ulcers present.

BACILLARY.

1. Acute in onset and running a rapid course.
2. Pyrexia common.
3. Ionic symptoms usually present.
4. Liver abscess never occurs.
5. Disease confined to the large intestine.
6. Ulcers usually formed on surface folds of intestine.

ETIOLOGY.—*Season.*—In temperate zones dysentery is far more common in summer than during the fall, spring, and winter, in the order mentioned. In the tropics, where the seasons are marked according to rainfall, the temperature being more equable, the incidence of dysentery is greater after torrential rainfalls, the probable explanation being the pollution of sources of drinking-water.

Soil.—Infected soil may continue to harbor the specific organism and give rise to recurrent outbreaks; how long it remains viable in soil is not definitely known. Both in temperate and tropical regions, marshy soil seems more prone to invite outbreaks than dry regions. Fecal pollution is naturally a most important element.

Food and Drink.—Famine or the use of improper foods, this latter especially in the tropics, may determine outbreaks. Fecal pollution of drinking-water or the transference of infection to food by flies are self-evident possibilities in causing more or less widespread outbreaks.

Exhaustion and Exposure. — Insomnia, prolonged and exhausting effort or profound worry, all play a rôle. Fatigue for any reason and severe exposure may so lower resistance as to encourage the development of dysentery, which, under these conditions, is apt to carry with it a high mortality.

> Dysentery in the Madras prisons has accounted for the majority of deaths during the past forty years. Many diseases reported as debility, anasarca, etc., and now not recognized as such, were in reality dysentery. Scarcity of food and bad food predispose to dysentery both outside and inside the jails of the presidency. C. F. Fearnside (Indian Med. Gaz., July, 1905).

Other Diseases.—Dysentery may occur as a terminal infection among the aged or children, especially in institutions, or it may complicate depraved states during the course of or as a terminal infection in other diseases, as in pneumonia, tuberculosis, Bright's disease, cystitis, etc.

Age.—No age is exempt; even the fetus *in utero* has been found affected by Marckwald. (Münch. med. Woch., 1901, p. 1920). Children at birth have been found with an infection which developed during intra-uterine life, having been contracted from the mother who was ill at the time with dysentery. The summer diarrheas of infants have been shown by Duval and Bassett ("Studies from the Rockefeller Institute," 1904, ii) to be due to one of the varieties of the *Bacillus dysenteriæ;* so, too, with the cases of so-called asylum dysentery reported by Vedder and Duval (Jour. of Exp. Med., 1902, vi, No. 2), and with the institution outbreaks in homes for the aged. In the tropics a large part of the high mortality rate among children is due to dysentery.

Sex.—Not a factor *per se,* only in so far as habits and greater exposure increase the susceptibility of the male.

Race.—No racial predilection. All people of all ages in all climes would best express the situation, the general predisposing factors previously enumerated being the important determinants.

Occupation.—The working classes being more exposed through fatigue, dietetic restriction or errors, and poor hygienic environment than the well to do, are naturally more prone to the disease. In country districts the lack of sanitation invites a more ready development than in cities, while in those exposed to great heat, as engineers, firemen, and cooks, are more liable in consequence.

BACTERIOLOGY.—One time the colon group of organisms were believed to play a rôle in the production of dysentery, and it is possible that their increased pathogenicity in the presence of inflammatory states of the bowel may add to the symptoms, but they do not occupy any direct relation in an etiological sense. Despite Shiga's painstaking work published in 1898 (Centr. f. Bact., 1898, xxiii, p.

599, and xxiv, p. 817), and almost at once confirmed by other observers, even in 1902 Bertrand (Rev. de. méd., July 10, 1902) stated his belief that dysentery was caused by an increase in virulence of the micro-organisms normally inhabiting the intestinal tract, and not to any specific germ. So, too, Booker believed with respect to the summer diarrheas of children. These he ascribed to a variety of bacteria, the most important in his opinion being the streptococcus and proteus vulgaris. Calmette (Archiv. de méd. navale, Sept., 1893) also found a coccus having all the properties of *Streptococcus erysipelatosus* and the *Bacillus pyocyaneus,* both regarded by him as causing dysentery among the natives of Cochin China. A similar enterocolitis has been described by Adami and Lartigau as occurring in the northern part of the United States and in Canada, and they also isolated the *Bacillus pyocyaneus.* L. F. Barker, of Johns Hopkins, and others have also reported several cases due to the same organism. Calmette succeeded in producing hemorrhages and ulceration of the stomach and intestines by the injection into rabbits of a culture of *Bacillus pyocyaneus.* Enteritis and enterocolitis are undoubtedly due in some instances to subvarieties of the colon group, notably the organisms of Gärtner and Escherich.

> There is a chronic form of dysentery due to the *B. coli communis;* these cases are not uncommon in the temperate climates. The form of infecting organisms does not correspond to the Shiga or the mannite-fermenting types; they are not possible of differentiation from the known forms of *B. coli communis* of high virulence. The serums from the writer's cases strongly agglutinated the organisms obtained from that patient and more definitely than they did the strains of *B. coli communis* ordinarily obtained and used in laboratory observations. The organisms existed in large numbers in the lower intestinal tract of the patients, mostly in the mucus, and were capable of destruction of tissue locally. Bassler (Med. Rec., Oct. 7, 1911).

The first studies of a definitely practical character, however, emanated from Shiga, as already stated. In his paper in 1898, on the epidemic form of dysentery occurring in Japan, he insisted that an organism, to be regarded as the direct cause of dysentery, must be constantly present in cases of dysentery, yet not normal to the host, and that it should be pathogenetic and capable of causing lesions in experimental animals similar to those occurring in the one from which the culture was made, and, finally, in man, it should agglutinate with the blood of those suffering from the disease.

Of late years the view has become more generally accepted that no organism is under all conditions fixed and definite, but that gradations exist, so to speak. For instance, from the colon group on the one end, to the typhoid group on the other, innumerable variations pertain; so, too, with the streptococci and all other micro-organisms. Nor is the dysentery bacillus an exception. Here, too, a group arrangement exists, in which the individual members present minor but appreciable differences. Two predominant types, however, have been described, the first by Shiga, which was isolated from the patients suffering with dysentery in Japan, and the second Flexner obtained from dysenteric cases in the Philippines. This is spoken of as the Flexner or Manila type. It has since been shown, however, that both of these types occur not only in Japan and the Philippines, but also wherever dysentery occurs, and that the two types may even be associated in the same individual. No differences can be detected in the morphology of various types. They are rod-shaped, rather short, somewhat resembling the typhoid bacillus, though a little fuller and the ends are round. Duval and Vedder were able to demonstrate flagella, but it is now generally accepted that only very young cultures develop motility in the organisms. They stain readily, often irregularly, and decolorize by Gram's method. They grow readily upon the culture media most commonly employed in laboratories, the growth being best obtained at a blood temperature. They do not peptonize. They do not coagulate milk, which becomes at first slightly acidified and later amphoteric or faintly alkaline, indol production being present in some and absent in others. Probably the widest differences exist in their fermentative properties, though gas is not formed in any of the sugars. They also differ in their property of agglutination. This is so marked that Kruse was led to describe what he termed true and false dysentery bacilli. This is, however, unjustifiable, as all of the species of virulence of a common type and the variation in agglutination are but a matter of degree. It has been found that the power to produce agglutination may be increased by successive cultivations on various media. It has been noted, however, that though cultivation is possible through perhaps several generations, it is not possible to continue them indefinitely. This varies with the type of organism, some showing a property of growth even after many transplantations. It may be stated, however, that the culture media should be slightly alkaline, as even minimal traces of acids seriously militate against the growth; consequently sugar media, particularly if fermentable, will not prove satisfactory, owing to the acids resulting from the sugars. The various organisms are not particularly resistant. They are at once destroyed by 5 per cent. of carbolic acid solution and 1:2000 corrosive sublimate. They are easily destroyed by saprophytes, and after ordinary conditions of soil or water contamination it is scarcely possible that they ever exist over two weeks.

The virulence of the various organisms is greatly diminished by culture. Though, as was shown by Marmorek in the case of streptococci, their virulence can be greatly increased by successive passage through laboratory animals, especially the guinea-pig. It seems, however, that an even greater degree of virulence can be obtained if intermediate cultures are made before transplantation from animal to animal. This seems peculiarly suggestive in the light of various outbreaks which occur from time to time, for it is probable that the organisms may be kept viable or have their virulence increased through the intervention of some of the lower animals.

Immunization has been shown to be practical in animals; but as each immune serum best protects against the type from which it was prepared, a therapeutic serum to be of any value had best be polyvalent, that is, made from many strains.

Human Bacillary Dysentery.—Owing to the rapidity with which the dysentery bacillus is destroyed, cultures should be made from perfectly fresh fecal material, though scrapings from the mucosa may be made at necropsy and growth will result if this be done within twenty-four hours after death. Careful selection should be made from the stool, preferably from clumps of mucus, with or without blood. This is placed in sterile salt solution or bouillon, thoroughly agitated or broken up with sterile glass beads, allowed to sediment for a few moments; then agar tubes may be inoculated successfully, the object being to effect dilution. These are then poured into Petri dishes and incubated at 37° C. for about eighteen hours. A very small, pearl-gray colony is then selected and transplanted by means of stabbing a glucose-agar tube. The plates should be kept at room temperature for purposes of further comparison, and the stab cultures should be examined after six hours at 37° C. Only those tubes are subjected to further subcultures and agglutination tests which fail to show gas-bubbles.

The discovery that the dysentery bacillus is the immediate etiological factor in dysentery, whether occurring in the tropics, subtropical or temperate zones, whether the disease occurs in epidemic form, institution outbreaks or sporadically, and, likewise, that it is the cause of the prevalent summer diarrheas of infants, naturally led to a query as to its source, mode of conveyance, and possible saprophytic character. These questions cannot be unequivocally answered at present. Except in those instances in which infection can be clearly traced from infected persons, its source and mode of transference are unknown. It is found in the recent fecal discharges of infected individuals and at necropsy; in the mucosa of the bowel, especially in the large intestine, where it penetrates into the crypts, but outside the body, it is rapidly overcome by other organisms. This latter fact, and its intimate relation with the mucosa, do not well accord with the view that it is adapted to grow elsewhere. It has been recovered from the stools of apparently healthy children by several observers; but as it may also be found in the stools of those apparently well, but exposed to infection during local or widespread outbreaks, just as cholera vibrio have been found in the stools of those exposed but unaffected during outbreaks of cholera, it cannot be denied that it may exist as one of the vast numbers of flora inhabiting the intestine of man, assuming pathogenetic properties under favorable conditions the nature of which we are at present in doubt. The prevalence of summer diarrheas of children and the etiological relationship to them which the dysentery bacillus group bears, and its similar intimate relation in causing institution and asylum outbreaks, argue for this hypothesis, and so too does the development of dysentery as a terminal infection in those in advanced stages of Bright's disease, chronic heart disease, diabetes, hepatic cirrhosis, malignant disease, and the like.

We know beyond cavil that pneumococci, various pus organisms, tubercle bacilli, meningococci, even typhoid bacilli, as well as the spirillum of cholera, as previously stated, may occur, some of them as constant inhabitants of the human body, without any evidence of morbid activity. It is very possible, therefore, that everyone is a "potential carrier," though in the more restricted sense carriers have only been proved to exist in the persons of those more or less recently actively infected. Local outbreaks have been traced to such individuals. It is not known how long the bacilli remain active in those who have had the disease, but there is no doubt that it may extend over many months.

> Carriers may be divided into two great classes. The first class consists of healthy persons, who have never suffered from the disease and show no signs of ill health, but nevertheless harbor and scatter the specific organism. In the instance of bacillary dysentery this class is small and unimportant. The author has never found a single case, but Conradi, Collins, and Mayer have been able to demonstrate such conditions in both children and adults living among those affected with the disease. In the second class are people who have had the disease and are thereafter unable completely to eliminate the infection.
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> As agents in the spread of the disease this second-class group cannot well be overestimated in importance. They consist of two groups, in the first of which convalescence is discovered only by the continuation of agglutination. They do not relapse, but they harbor infection somewhere, and an occasional stool contains mucus. The second group is of relapsing and chronic cases, a constant source of infection. Isolation, observation, and care during convalescence are necessary, as a means of prevention of spread of an epidemic. Unfortunately, these incomplete convalescents form a high proportion of the cases. Macalister (Brit. Med. Jour., vol. ii, p. 1506, 1910).

MORBID ANATOMY.—From the foregoing, in order to establish some type as a basis, it appears advisable to consider, first, the lesions occurring in the severer forms of dysentery of the epidemic type, for of their true nature there can be no doubt. With these in mind, it will be possible to correlate those cases occurring especially in temperate zones, not necessarily grouped, often isolated examples in fact, such as one meets with in the summer diarrheas of infants. Clinically, there are acute and chronic types of dysentery. The most marked lesions occur, as one would expect, in the epidemic and endemic forms, and, naturally, the severity and duration of the attack are factors which determine the extent of bowel lesion. In the most acute cases, where death supervenes after an illness of a few days, the mucosa of the large intestine is swollen, injected, often of a very deep red color. The process begins on the tips of the mucous folds, then spreads to other portions. Apart from this more or less general hyperemia, minute extravasations and hemorrhagic foci may be seen, and the wall soon becomes edematous and covered with mucus. A pseudomembrane forms almost at once, at first irregular, patchy, but may become general. Early in the stage of its formation it may be wiped off, but in all likelihood, owing to the activity of the various pathogenic organisms present, foci of ulceration occur. In the most intense cases these ulcers may penetrate to and even through the serosa, purulent peritonitis resulting. Usually, however, they dip down to the muscular coat. Mixed infection and dehiscence of the more or less necrotic mucosa and false membrane give rise to these irregular, often extensive ulcers. The solitary lymph-follicles are swollen, often softened and may break down. The small intestine, always less involved, is more or less hyperemic, and the ileum, which is the region of the small bowel most markedly affected, may present the same character of pseudomembrane, even ulceration, and the lymph-apparatus throughout the small intestine may become swollen and in the ileum necrotic, as was noted in the large intestine. In the less acute cases the loss of continuity of mucosa is small, mere erosions, but the hyperemia is marked. In chronic cases the bowel wall, especially the wall of the large bowel, becomes thick, indurated; the serosa thickened in patches, often pigmented, and the mucosa beneath also pigmented, mark the site of recent ulceration. Healing by cicatrization may slowly progress in areas, with ulcer formation in other places, and more or less distortion; even stricture may result, or the bowel function be permanently modified in consequence of the changes resultant upon the various lesions. The bowel wall may undergo amyloid change due to prolonged suppurative lesions. Microscopically, the pseudomembrane is seen to consist of fibrin, entangling erythrocytes, and cells undergoing degeneration, the whole upon a mucosa undergoing coagulation necrosis. Hemorrhagic extravasations and accumulations of Unna's plasma cells, small round cells, polymorphonuclear neutrophiles and eosinophiles, and more or less degeneration of submucosa and muscularis complete the picture. Abundant bacteria can be seen in appropriately stained sections, but cannot be recognized, except possibly the streptococci. The epidemic form, both in adults and children, presents a common type, but those forms of bacillary dysentery occurring clinically as summer diarrheas of infants vary much. There may be merely hyperemia and edema of the large bowel, much less marked in the small intestine, with or without pseudomembranous formation, while in others hyperplasia of the lymphatic apparatus constitutes the chief feature, and in some the pathological changes are very slight, scarcely amounting even to hyperemia.

The bowel lesion results, in all probability, not from direct action of the bacilli, but from their toxin, which is eliminated by the bowel, after absorption into the blood. Sweet and Flexner have shown that the toxin enters the intestine in large part with the bile, for in experimental animals possessing a biliary fistula, lesions of the bowel are either prevented or at most are very trifling in character.

PROPHYLAXIS.—It is of importance to avoid the use of alcohol, in the tropics especially. Even in temperate zones the intemperate seem more prone to infection. All discharges from a patient should be disinfected. Neglect of this procedure may invite a widespread outbreak, especially where subsoil and water contamination are possible. Fatigue and exposure to heat or dampness increases one's susceptibility. Flies may spread the disease unless the dejecta are covered prior to disinfection. All excesses in food or the use of uncooked vegetables, celery, cress, salad or fruits may act as predisposing factors, or the uncooked foods may actually be the means of direct infection through contaminated soil, just as we know them to be in the case of typhoid fever. The value of serum from horses immunized against dysentery, as well as bacterins, used prophylactically, are too recent to permit of an authoritative statement.

> Bacillary dysentery should always be a reportable disease, and health authorities should have full power to investigate and abate any suspected source of this disease. The nomenclature should be broad enough to include all types of the disease; bacillary dysentery will include dysentery and paradysentery. Varied diagnoses such as "diarrhea," winter cholera," "intestinal grippe," "grippe," "gastric fever," "intestinal disorder," and many others evidence an apparent, notable ignorance of the etiology and probably of the pathology of cases infected by members of the dysentery group, resulting in a longer continuance of the infecting source and a higher mortality. When casually associated with *Bacillus typhosus,* epidemics of bacillary dysentery may be followed within ten to twenty-one days by an increased number of typhoid-fever cases. This happened in 5 out of 9 instances in Pennsylvania, and may serve as a warning of the presence of the more serious infection; a decrease in the morbidity and mortality due to typhoid fever would follow the abatement of the sources. Hunt (Jour. Amer. Med. Assoc., Sept. 21, 1912).

TREATMENT.—Whether mild or severe, acute or chronic, absolute **rest in bed** is necessary. A firmly applied **flannel binder** should be employed, with or without **hot applications to** the **abdomen,** either dry or moist, and the patient kept warm and free from all sources of irritation. Thirst is a very annoying symptom, but if the patient is vomiting absolutely nothing should be given by mouth. Fluid may be administered by **hypodermoclysis** or, if the rectum will tolerate it, by **enema.**

The **diet** is an important factor. Those who take it well should be given predigested milk or whey, but special care should be exercised to insure milk beyond suspicion. Lime water or barley water may be added with advantage, unless the milk is predigested. Rice, barley or oatmeal water or albumin water, strained gruels or chicken or other meat broth thickened with some cereal and strained should constitute the sole diet of those unable to take milk or as variants with a milk diet. All alcohol should be avoided except where prostration is marked, when **wine whey,** or **brandy and milk** may be given, also **aromatic spirits of ammonia** with a drop or two of **chloroform** in ½ dram (2 Gm.) of **Hoffman's anodyne.** Even after convalescence has been established, it is important to maintain the greatest care in the matter of **diet,** adding very gradually the cereals, vegetables, and finally the meats.

Early in the course of an attack, **salines** may be given, **Glauber's** or **Rochelle salt** in one dose of ½ to 1 ounce (15 to 30 Gm.) in the morning, or, if free purgation with a change in the character of stools is not produced, this may be repeated at four-hour intervals for twelve to twenty-four hours. One dram (4 Gm.) every hour may be given instead of the above. In some instances this will effect a prompt disappearance of blood and mucus. In the more severe forms this method usually fails and in the gangrenous stage should not be employed at all. **Castor oil** in 1-ounce (30-Gm.) doses may be given and repeated in eight to twelve hours, or **calomel** may be given in a single large dose, followed in six to eight hours by a **saline.** Repeated doses of calomel are apt to add to the misery of an already inflamed anal region and rectum. Small doses of **bichloride of mercury,** gr. 1/100 to 1/60 (0.00065 to 0.001 Gm.) may be given every two hours.

Large doses of one of the **bismuth** preparations with **paregoric** or **laudanum** by mouth will often give some comfort, but it seems wiser to employ **morphine** hypodermically in doses of gr. 1/4 to 1/3 (0.016 to 0.02 Gm.) in an adult, every three or four hours for the relief of the tormina and tenesmus. When the tenesmus is urgent, a **suppository** of **cocaine** or **opium** may be used, followed by a low **starch-water enema** containing about 30 drops of **laudanum,** or **bismuth** suspended in acacia solution may be used. While **ipecacuanha** and **emetine** (see article on EMETINE, this volume) are of less value in the bacillary form than in amebic dysentery, they may be tried, but unfortunately no single medicinal treatment will give the same result in every case. When given from the beginning of an attack these two agents are apt to be of most service, though even in well-marked and severe cases, especially in the catarrhal stage, they sometimes act well. If the patient has been previously constipated, a dose of salts or oil should be given first. Nothing should be given by the mouth for several hours preceding the **ipecacuanha,** which is best administered at bedtime in salol or keratin-coated pills, to insure their passage into the duodenum before solution occurs, lessening the likelihood of nausea and vomiting. From 60 to 90 grains (4 to 6 Gm.) may be given at the first dose, less each evening for a week, then daily doses of 1/2 dram (2 Gm.) in divided doses should be given for at least two or three weeks. Where the pills cannot be prepared one may give 30 to 60 grains (1 to 2 Gm.) of the powdered drug in the form of a bolus, to be repeated every six to eight hours. If vomiting occurs it may not render subsequent administration impossible. Precede the dose by placing a **mustard plaster** over the epigastrium and give a hypodermic of gr. 1/4 (0.016 Gm.) of **sulphate of morphine** or **laudanum** ♏xxx (1.8 c.c.) by mouth. When the passages begin to show fecal material, betterment is near at hand and the dosage and frequency should be reduced, but 20 to 30 grains (0.3 to 2 Gm.) a day should be continued for a couple of weeks. For children, much smaller doses should be employed. It is not to be given to pregnant women without explaining the risk of abortion from possible repeated vomiting, nor to those who for any reason are devitalized, as the actively tuberculous, for instance.

> **Ipecacuanha** is credited with quite a specific action. It does not curtail the course of the disease in many cases, but, on the other hand, requires careful use on account of its emetic action. It should be given on an empty stomach, and as this drug is much tolerated in dysentery, a dose of about 30 grains (2 Gm.) of the powder is necessary every four to six hours, until the motions become yellow and less slimy.
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> Such drugs are salol, or chlorine in solution, do not produce the same happy result as sometimes occurs during their use in enteric fever.
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> Once the acute stage is passed and the digestive powers return, the patient's strength must be well maintained, and such additional support

as eggs and finely divided raw meat may be allowed. The stage of convalescence being well established, tonics become useful, and to accomplish the necessary improvement in health a **sea voyage** or **change of climate** is necessary. E. L. Jenkins (Brit. Med. Jour., Aug. 12, 1905).

The **ipecac** treatment of dysentery caused by protozoa should not on light grounds be set aside in favor of any other, but in using this treatment great care should be taken to make sure that the dysentery is truly caused by protozoa and is not bacillary, and also to obtain an ipecac that is shown by actual analysis to contain its proper amount of emetin, and, when this is not possible, to insist upon obtaining the Brazil root. E. B. Vedder (Military Surgeon, Sept., 1911).

Whenever possible, **enemas** should be resorted to. Even though the anal region be irritable, a suppository of **cocaine** and **opium** will usually obviate all pain or, at least, make it bearable. A preliminary **enema** of physiological **salt solution,** 2 or 3 quarts, should be given, the patient lying on the right side, hips elevated, and head low. This is to be followed by an **enema** of 3 quarts of a 1 per cent. solution of **quinine bimuriate with urea.** This causes some pain at first, but its anesthetic effect is soon felt and, being to some extent a parasiticide, it has a double range of usefulness. Since in many cases the disease is confined to the large bowel, the involved area can be thus directly treated. In well-advanced cases where there is likelihood of softening and extensive ulceration of the bowel wall, enemas are contraindicated, as the risk of perforation cannot be denied. Nor would they be of value in treating that part of the morbid process when the small bowel is involved. Saturated **boric acid solution** or a 1 per cent. or 2 per cent. **solution of salicylic acid** are distinctly of less value than quinine enemas in any case. Any enema employed should be given at body temperature.

The writer urges the value of intestinal irrigation over internal medication in the treatment of dysentery. He uses a hot **boric acid solution,** containing 1 dram of boric acid with a pinch of **sodium carbonate** to 1 ounce of water, **massaging** the abdomen gently during the irrigation. Internally he uses the bark of **Holarrhenœna antidysenterica,** a small, bushy plant very common in southern India, whose native name is pandarakorda. The bark of the root only is used. It is macerated in sour whey, one wineglassful of the solution being taken four times a day. It is pleasant to the taste and is carminative and diuretic. This drug is far superior to ipecac. Desai (Jour. of Tropical Med., Nov. 15, 1905).

Advocation of the use of strong solutions of **silver nitrate** in the treatment of acute dysentery rather than those ordinarily recommended. Injections of a 5 per cent. solution of silver nitrate were used for the treatment of 10 cases. The treatment was instituted at an early stage, from the second to the fourth day of the disease as so judged by the appearance of symptoms. The average duration of these 10 cases was ten days and the maximum duration, seen in 1 case, was fourteen days. The writer gives the details of the treatment as follows: The patient when first seen was given a dose of **magnesium sulphate.** As soon as this drug had acted, irrigation by **silver nitrate** was given. The rectal tube was inserted from eight to twelve inches and a pint or more, according to the capacity of the patient to hold the solution, of 5 per cent. silver nitrate was injected. The injection was retained by the patient as long as possible, up to a half-hour. Defecation was then allowed. Rectal injections of **salt**

solution were given regularly after each movement during the course of the treatment. A second injection of silver nitrate was, as a rule, given after a period of two days. In some cases one injection only was used. A **diet** selected with the idea of reducing the amount of fecal food residue was given. The daily content of this diet was as follows. Lean meat, 300 Gm.; three slices of toast with maple syrup; albumin water consisting of the white of 8 eggs in water. This was continued for five days. The diet was then increased by the addition of more toast, butter, tapioca, potato juice, and macaroni. Hewes (Boston Med. and Surg. Jour., vol. clxii, p. 530, 1910).

Serum therapy has a limited range of applicability, but has been of some value when employed in the early stages. Shiga has prepared an immune serum, so called, by repeated injections of polyvalent strains of the dysentery bacillus into a horse. Doses of 20 c.c. to 30 c.c. of the immune horse serum should be injected two or three times a day for several days, smaller doses in children.

Serum of horses immunized against the bacillus of dysentery possesses antimicrobian and antitoxic properties which render it useful in therapeutics. This serum is proving to be almost specific in the treatment of bacillary dysentery. It has no effect on any other variety. It arrests both the infection and the intoxication and insures rapid recovery, putting an end at once to all the intestinal disturbances. Its effects are more striking the earlier it is used, although it has proved effectual even as late as the sixteenth day. Prolonged and chronic dysentery is also amenable to this serum treatment. These results were practically constant in 96 cases of severe dysentery treated with the serum alone, the number of stools ranging from 15 to 288 a day. The amount injected ranged from 20 to 100 c.c., and the injection was sometimes repeated after twenty-four hours, and again a third time in the most threatening cases. The Shiga-Kruse bacillus had been used to immunize the horses, but the serum proved equally effectual against this and against the Flexner bacillus. The curative action of the serum is so prompt and certain that its prophylactic use seems hardly necessary. Vaillard and Dopter (Annales de l'Inst. Pasteur, vol. xx, No. 5, 1906).

Polyvalent antidysentery serum was administered to 13 children by the author; in 2 the dysentery was caused by the Shiga bacillus, and in the others by the Flexner bacillus. The mitigation of the symptoms after the injection of serum was so rapid and so evident that the efficacy of the serum seemed to be beyond question. All the patients promptly recovered. P. Coyne and B. Auché (Bull. de l'Acad. de Méd., Oct. 1, 1907).

Series of 15 cases treated with **serum** from a horse immunized with filtrates of three-week cultures of the Shiga bacillus. In the course of a year, 1280 c.c. had been injected; the curative serum obtained had a purely antitoxic action. Slight if any by-effects were observed, though curative results were obtained. T. Skschivan and W. Stefansky (Berl. klin. Woch., Bd. xliv, Nu. 6, 1907).

The **serum therapy** of dysentery was begun by the writer in 1903. He first injected horses with killed cultures of a dysentery bacillus which he obtained in Japan, and later injected living organisms. Todd then elaborated a pure, antitoxic serum by injecting horses first subcutaneously and then intravenously with dysentery toxin. Other investigators, among whom may be mentioned Kruse, Vaillard, Dopter, Krauss and Doerr, confirmed these findings. By means of serum therapy the mortality of diseases was reduced to less than 17 per cent. of the former death rate. Since 1906 numerous investigations along the lines mentioned were carried out. Horses were injected intravenously with a mixture of various strains of domestic dysentery bacilli. Alkaline broth was first injected under the skin, and then intravenously. The injections were made every two or three weeks, since it was determined that injections of shorter intervals frequently killed the animals. Commencing with an initial injection of 0.1 c.c. of the culture, the amount injected was increased until finally as much as 100 c.c. could be given. In the beginning a larger number of the horses were killed by anaphylactic phenomena, but later this result was avoided by the anti-anaphylactic method of Besredka. The entire immunization stretched over a period of eight months. The horses are then bled, 8 liters of blood being withdrawn every four days until 24 liters of blood are taken. The horses receive a rest of about twenty days, and the injections are then begun again. The serum is preserved with 0.5 to 1 c.c. trikresol. The serum obtained from the blood will give agglutination up to 1:1000 immediately, and 1:2000 within three hours. It was possible by means of an antigen prepared from dysentery bacilli to obtain complement fixation. The antitoxic value of the serum was obtained by first determining the lethal doses of old and fresh cultures of Shiga bacilli and then injecting various mixtures of the toxin and antitoxins. Animals injected with the mixture did not succumb. It was possible by means of 1 part of serum to neutralize ten times as much toxin. These experiments were carried out on rabbits, and it was determined that the protective properties of the antitoxin were definite and unmistakable. M. Shiga (Ann. de Biol., t. i, No. 2, 1911).

The results recently obtained with **serotherapy** in the Shiga type of dysentery in eastern Austria are fully on a par with those of the antitoxin treatment of diphtheria. The writer has recently controlled 2000 cases during the past year. This could also be contrasted with a large number of cases otherwise treated. The mortality of the cases treated with **antiserum** was between 9 and 10 per cent., while that of the material otherwise treated was between 19 and 20 per cent. One condition of success was that the serum be given as early as possible, when its beneficent action was at once evident in the abortive course of the disease. The serum is essentially antitoxin. Krause (Deut. med. Woch., March 7, 1912).

Case of bacillary dysentery in which, ordinary medicinal measures failing to benefit, the patient, a child, became extremely thin and was obviously sinking slowly. Examination of the stools revealed the presence of the dysentery bacillus, type y. The serum corresponding to this type not being at hand, 1 c.c. of Shiga's **serum** was given hypodermically. The temperature fell immediately from 39° C. (102.2° F.) to 37.4° C. (99.3° F.) and remained at about 37.5° C. (99.5° F.) for two days. After a second injection the temperature fell to normal in forty-eight hours, and the child, previously suffering extremely from sleeplessness, at once obtained rest. A third injection of 1.5 c.c. was given. The stools showed marked improvement, and convalescence took place gradually but uninterruptedly. The writer concludes that since the Shiga serum proved so beneficial, the different types of dysentery bacillus must be nearly related, and that in case of emergency it is worth while to use the serum appropriate for one type in the treatment of disease caused by the other. Graham (Jour. of Trop. Med. and Hygiene, June 15, 1912).

A serum is also furnished by the Pasteur Institute and the Lister Institute. The injection of attenuated and dead cultures into the bodies of laboratory animals confers an active immunity upon them, but the injection of dead bacilli (**bacterins**) into man causes a sharp local reaction after the first dose, with more or less constitutional disturbance in most instances and some febrile reaction, just as we know it in the case of prophylactic injections of typhoid bacterins. They have not been employed sufficiently to enable one to speak with any degree of certainty as to their protective value, and again as, in typhoid fever, bacterins used therapeutically are almost without influence and certainly of no demonstrable clinical value. (See article on BACTERIAL THERAPY in the first volume.)

> A **vaccine** can be prepared from the Shiga bacillus, which in therapeutic dose gives rise to no greater discomfort than a little local tenderness. The vaccine employed consisted of an emulsion of the dead bacilli in normal salt solution, to which 0.5 per cent. of carbolic acid had been added. The vaccine is injected subcutaneously in line with the outer border of the rectus muscle, half an inch above the umbilicus. W. H. C. Forster (Indian Med. Gaz., June, 1907).
>
> Experiments on the **vaccination** of full-grown mice by feeding them with bacilli of dysentery of the Shiga type, both living and dead. One single ingestion of this dose is insufficient to bring about immunization, and that it is only conferred with weaker doses when they are repeated daily for a week. The immunity is not complete until about the end of twelve days and it usually lasts for a month. From the first to the twelfth days, while the state of immunization is in process of development, a "negative phase" is induced, and the animal is more sensitive than the control mice to an ordinary fatal dose. Similar results were obtained with living bacilli. M. Dopter (Lancet, June 6, 1908).

Chronic Dysentery.—**Rest** in bed, a very simple **diet** of farinaceous food, creamed potatoes, cereal broths, peptonized milk, gruel and eggs. Milk is often poorly borne, and, even when peptonized, curds may form and add to the irritation present. In such instances give no milk at all. Boiled, aërated water or pure water from any source may be given, unless there is much vomiting; then give nothing by mouth. **Bismuth** and **opium** are the best drugs to give, but, on account of the chronicity, a word of caution against the possibility of forming the opium habit.

Rectal and **colonic irrigations** are of great value; the same caution to be observed as in acute cases.

> Eleven cases of dysentery were successfully treated with **irrigation** of an emulsion of **creosote** prepared by adding to a quart of water, with which the yolk of an egg has been mixed, a dram of 10 per cent. creosote. Billet has also employed creosote irrigations in dysentery due to the *Entameba hystolytica* of Schaudinn. He gives irrigations of from 1 pint to 1 quart (½ to 1 liter) of 1 to 2 per cent. creosote, which has been previously mixed with oil of sweet almonds, in water. Usually two enemas a day are given. In a large majority of the patients thus treated, the pain is rapidly relieved and the blood and the fetor disappear from the stools. G. Zanardini (Semaine méd., vol. xxvi, p. 462, 1906).

Though less frequently indicated than in amebic dysentery, it is the chronic type of the bacillary form in which an **appendicostomy** and subsequent **intestinal lavage,** through the stump promises beneficent results.

> The writer was much gratified with the results of treatment with **ipecac** given with a few drops of **opium** and **peppermint,** supplemented by **high rectal injections** of about 250 c.c. (½ pint) of a solution of 5 Gm. (1¼ drams) **iodoform** in 1000 Gm. (3⅓ ounces) of **mucilage of gum arabic,** given in the knee-elbow position

under high pressure, with an attempt afterward to massage it up into the colon. The iodoform is left in the intestines for about ten minutes and the larger part is then washed out with two enemas of water. If the amebæ are ensconced in the appendix it may be necessary to remove that structure before the affection can be cured. Meyer (Deut. med. Woch., Bd. xxxii, Nu. 33, 1906).

In the treatment of chronic dysentery **appendicostomy** should be given preference over cecostomy unless there is some obstacle to its performance. The writer treated 31 cases of chronic amebic dysentery, chronic colitis, following acute dysentery. The oldest case had existed eleven years. Appendicostomy followed by irrigations gave satisfactory improvement in the symptoms, but did not suffice to produce cures. In the amebic cases the parasites rapidly disappeared. In 5 cases cecostomy was performed. The openings must not be allowed to close or the dysentery returns. Weakening of the abdominal walls with the formation of ventral hernia occurred in 8 (25 per cent.) of the cases. W. D. Webb (The Post-Graduate, Aug., 1910).

AMEBIC DYSENTERY.

Amebic dysentery, or amebiasis as it is also called, is an acute or chronic, ulcerative disease of the colon due to the *Entameba histolytica,* with a special tendency to the production of abscess of the liver, usually large and single; less often, small, multiple abscesses.

SYMPTOMS.—The disease manifests itself in an acute and chronic form.

Acute Type.—In this variety the onset is sudden and sharp and the course acute. Without an examination of the stools it would not be possible to differentiate it clinically from bacillary dysentery. This may be the explanation of the statement that acute amebic dysentery is a somewhat rare condition. The patient is more or less abruptly seized with abdominal pain—tormina and tenesmus. The degree of tenesmus and frequency of stools are directly proportionate. The stools are bloody or blood-streaked mucus is passed, and in a few days they become copious, watery, of a dirty brownish-red color, and contain flocculi or shreds of tissue, and they often have an intensely fetid odor due to the gangrenous sloughs therein.

Four cases in which the fatal termination was due to intestinal hemorrhage. In all the cases large liver abscess coexisted, thus showing a close causal connection between the two and the hepatic condition. While it is probable that more extensive observations will show that fatal intestinal hemorrhage in amebic dysentery may occur quite independently of liver abscess, the cases witnessed by the writer seem to show that when hemorrhage occurs in cases complicated with such hepatic disease it is likely to be very severe and that the bleeding is likely to recur. Strong (Amer. Med., Jan 27, 1906).

Case of amebic dysentery with abundant hemorrhages and a peculiar nodular form of ulceration. Several such have been recorded. The large intestine contained a large amount of dark-red, almost black, pasty material in which amebæ were numerous. From the ileocecal valve to the lower part of the rectum the mucosa was studded with nodular elevations which varied from six to twelve millimeters in diameter and which rose about an equal distance above the level of the mucosa. In most cases the elevation was surmounted by a mass of necrotic tissue which could be scraped off, leaving a deep, crater-like ulcer extending well down through the mucosa. Only one or two small typical, irregular amebic ulcers were observed. Many active amebæ were found in the detritus taken from the crater-like ulcers. H. T. Marshall (Philippine Jour. of Sci., Oct., 1909).

Rapid loss of flesh and strength occurs; indeed, it is seldom that such extreme emaciation occurs as is noted in many of these acute amebic dysenteric cases. The heart becomes increasingly feeble, weak, and rapid; the temperature for the first few days ranges from 99° F. to 102° F. or 103° F. (38.9° C. or 39.4° C.), but often falls even below normal toward the end, and death may result from exhaustion within a week, or a copious hemorrhage from the bowels or perforative peritonitis may cause death. Many patients recover however, and some pass into the chronic form. Among those who survive, diarrheal disorders are common and occasionally cicatricial contraction of the bowel and final obstruction may occur.

Chronic Type.—In most cases the disease runs a more or less chronic course, in which the chief characteristic is attacks of alternating constipation and diarrhea. During the diarrheal periods there may be a little fever, abdominal pain and tenesmus, with some mucus or bloody mucous stools. General nutrition is well preserved. The tongue is apt to be red, beefy, the appetite impaired, and little inclination toward effort of any kind is often noted.

The duration is variable, months to several years. Some of these chronic cases may be spoken of as masked or latent, for infected individuals may harbor amebæ for long periods without being conscious of it.

The writer reports cases of infection with *Entameba tetragena* which illustrate the production of cysts by this organism, its intermittency, the absence of cysts during acute symptoms, and their presence in formed stools long after the subsidence of acute symptoms. Infection in man appears to be the result of contamination of food with a small amount of fecal matter containing a great many cysts, during the first day or two after passing.

The great importance of examining the stools of all convalescent and recovered patients with entamebic *dysentery* for cysts and thus detecting "carriers" is apparent, for it is the cyst that is the infecting agent and not the large trophozoite. S. T. Darling (Archives of Intern. Med., Jan., 1913).

The indisposition may be slight and not such as to direct attention to the intestinal tract, except abdominal pain be present. Liver abscess may develop insidiously, and one of the complications may be the first evidence of the serious state of the patient.

COMPLICATIONS.—The most frequent and one of the most serious complications is hepatic abscess. Rogers believes that it is preceded for a variable period by fever of intermittent or remittent type, sweats more or less marked, leucocytosis, and an enlarged and tender liver. If the hepatic enlargement is irregular, dome-shaped, the condition is more readily recognized, but quite often the liver is uniformly enlarged.

Hemorrhage, perforative peritonitis, or peritoneal adhesions and displacement of abdominal organs may result. Other infectious diseases—as typhoid, malaria, tuberculosis—may be associated with amebic dysentery, or amebic and bacillary dysentery may occur in the same individual or other intestinal parasites may be associated.

DIAGNOSIS.—The most important aid to diagnosis is the finding of amebæ in the stools. If these are actively motile with well-marked pseudopodia, with a scarcely demonstrable nucleus, the probability is we are dealing with an amebic infection; but as non-pathogenic amebæ are not uncommon, in liquid stools especially, too much stress should not be laid solely on the finding of amebæ. The agglutinin test will rule out bacillary dysentery. In the tropics, all cases of diarrhea, however slight, should be looked upon with suspicion until patient, careful examination removes the doubt. The outline of the liver should be mapped out frequently. If it undergoes any change in size with or without change in shape, especially if chills, fever, and sweats exist, an abscess of the liver has probably developed. The leucocyte count is of some value. Not over 10,000 to 15,000 white cells are found in the average case of uncomplicated amebic dysentery; when liver abscess occurs, the count goes up to 20,000 or 30,000.

Out of 300 examinations of feces, made as part of the regular laboratory routine at the Canacao Naval Hospital, P. I., only 20 were admitted on the diagnosis of dysentery. The writer concludes that, reasoning from a knowledge of the power of other forms of intestinal parasites to produce symptoms of a general nature, such as those mentioned, and taking into consideration the reported findings at autopsy in many cases of amebic infection without apparent symptoms of dysentery, it would be unwise to ignore this organism as an etiological factor in affections other than dysentery. Hoyt (N. S. Naval Med. Bull., July, 1908).

It is important to determine whether or not the complement fixation test in the tropics would be interfered with by any of the diseases common to such latitudes. For various reasons the Noguchi modification of Wassermann's method was employed. The writer found that the hemolysis was not interfered with in malaria, filariasis, amebic dysentery, or yellow fever. In the latter the presence of biliary substances had no effect. In yaws a positive Wassermann reaction was obtained, also in leprosy, but in this disease, on account of a certain similarity in lesions, a diagnosis of syphilis could not be made positively. It was also interesting to note that a positive reaction was obtained in about 40 per cent. of cases of arthritis, free from other syphilitic lesions. Bates (Trans. Amer. Med. Assoc.; N. Y. Med. Jour., June 8, 1912).

ETIOLOGY.—*Geographical Distribution.*—Prevalent throughout the tropics, amebic dysentery is especially common in Egypt; indeed, it is almost the only form of dysentery met with in that country. It is less common in other parts of the African continent, and in India too its frequency varies greatly in different parts. It is very common in the Philippines. In the tropics it is constantly present and may even be said to exist in epidemic form at times. Of special interest, however, is the fact that it occurs sporadically in any part of the temperate zone, though but very few cases have ever been rported from England. It is common in the United States, especially in the Southern States at low altitudes, near the sea level. Osler states that the cases of acute and chronic dysentery admitted to the Johns Hopkins Hospital have been almost exclusively amebic, and that of 182 cases up to the year 1908, 123 came from the State of Maryland.

Case of sporadic dysentery in a robust young woman who succumbed to chronic marasmus, the result of an acute dysentery. She resided in Berlin and was taken sick after a trip to Silesia and Breslau. The intestines showed the necrotic processes characteristic of tropical dysentery, and the true dysentery ameba, Schaudinn's histolytic ameba was cultivated from the stools. Albu (Zeit. f. klin. Med., Bd. lvi, Nu. 5, 1905).

Fatal case of amebic dysentery that occurred in a man aged 42, who had never been away from the Birmingham district in England. The chief points of interest in the case were: (1) Ulcerative colitis, in which the smaller ulcers are circular and flask-shaped—*bouton de chemise* of French authors—with overhanging edges and relatively small circular openings into the lumen of the bowel, and adherent sloughs; one of the larger ulcers had perforated into the peritoneal cavity. (2) The presence of an enormous abscess in the posterior part of the liver, the pus of which gave no growth on inoculating in ordinary media. (3) Last, and most important, the presence of amebæ in the ulcers and the liver abscess and in the tissues around these lesions. As to the mode of infection, the authors point out that, given a case of tropical dysentery—and such cases are from time to time imported into England—there is a possible source of infection from wrich contamination of food or drink during warm weather might take place. As the ameba readily dies at temperatures below 75° F. (23.8° C.), it rarely spreads, even when imported. Saundby and Miller (Brit. Med. Jour., March 27, 1909).

It was recently believed that amebic dysentery was purely a tropical disease or acquired only in those regions. A theory has been suggested that cases occurring in our climate are due to eating uncooked tropical fruits on which the ameba had been imported. There is no scientific evidence in the support of this theory and cases occur in which its possibility can be excluded. The writer and Dr .Mathews, have had half a dozen such cases under their care in the past few months, two of which are reported. In both of these the evidence was strongly in favor of impure drinking-water as the cause. Amebæ are indigenous in this country, but the less favorable environment than in the tropics renders them less in number and virulence, and the disease caused by them is consequently rarer and less severe. G. S. Hanes (Jour. Amer. Med. Assoc., June 19, 1909).

Seasonal Influences.—For some unknown reason the incidence of the disease varies, so that even in the tropics in certain years bacillary dysentery may prevail, while in other years amebic dysentery will constitute the larger number of dysentery cases, and, of course, it is not an uncommon thing to find the two associated. In the temperate zone amebic dysentery is most apt to occur in its active manifestations during the warm months.

Age. — Probably owing to the greater opportunities for infection, it is much more common among young adults, and especially is this true where troops are stationed. Children readily become infected, but, as a rule, less severely than adults.

Sex.—Far more common in young adult males, both in the tropics and in the temperate zones. Of Osler's 182 cases at the Johns Hopkins Hospital, Futcher states that 171 were males. One reason for this, and that a very important one, is that women are more temperate in their habits and less apt to be exposed to the direct cause of the infection. Exposure and fatigue increase one's susceptibility; hence the likely explanation for its frequency among troops.

Race.—The white race would seem to be more susceptible than the black, according to Osler, also more susceptible than the natives of the tropics, and the disease is more amenable to treatment in the latter. This may be more apparent than real, however, because long residence acclimatizes them, and possibly active infections overcome may increase the resistence of the native race. Certain it is that the Caucasians live under better sanitary conditions than the natives, yet gastrointestinal and hepatic congestions are the rule among the Caucasians in the tropics, and especially is this the case with those who use alcohol freely.

The Direct Exciting Cause.—The **amebæ** were first discovered in 1859 by Lambl, in the stools of a child suffering with "enteritis," but he did not consider them of pathogenic import. They were again noted some years later, both by Cunningham and Lewis, in the stools of cholera patients and even in the stools of apparently healthy individuals. The name, *Ameba coli,* was first conferred by Lösch, who in 1875 found the organism in the stools of a chronic dysenteric patient who, at necropsy, was found to have extensive ulceration of the colon. He claimed for them in part only an etiological relationship with dysentery. He described them minutely as to shape, size, and character of motility. He, too, found that they succumbed to the use of enemas consisting of a solution of **quinine**, of a strength of 1:5000. Lösch attempted to reproduce the disease in dogs. He injected fecal material containing *Ameba coli* in the rectums of 4 dogs. In 1 of them he found amebæ eight days later, and in another, which was killed on the eighteenth day, he found rectal swelling, injection, and slight ulceration. Later, many attempts have been made by a number of observers to produce the disease in cats and dogs by means of rectal injections with fecal material, and the cat especially has been shown to be quite susceptible. Kruse and Pasquale retained the enema in the experimental animals by placing a stitch through the anal structures. To obviate much if not all of the bacterial infection resulting from injections of fecal material, they later used the necrotic material obtained from the liver abscesses of amebic dysenteric patients, and under both conditions obtained pathological changes mimicking those resulting from the disease in man, and they also found the *Ameba coli* in the bloody, mucous discharges from the bowel. Marchoux succeeded in producing the disease in a number of cats. Those which lived over fifteen days developed hepatic abscess, single as a rule, occasionally multiple. It was found that a temperature of 45° C. will destroy the ameba, but does not harm the bacteria. Material so treated when injected proved negative. Harris failed to produce the disease by injecting cultures of all recoverable flora from a case of amebic dysentery, but did succeed in inducing it in a puppy, by an injection of fecal material from the same source, containing amebæ. A liver abscess also resulted. This seems conclusive evidence that an ameba exists with pathogenic properties capable of causing both dysentery and hepatic abscess.

It is to Robert Koch, however, that we are indebted for our first definite knowledge of the parasitic properties of the organism. While investigating cholera in Egypt in 1883, he found them in the deeper portions of ulcers in the intestines of several cases of dysentery, and because of their deep position he looked upon them as exercising a causal relationship. It was his influence which led Kartulis to study them. Kartulis found amebæ in the stools of over 500 cases of dysentery in Egypt, and he also found them in the necrotic contents and walls of liver abscesses complicating that disease. He observed, too, that their number was seemingly related to the severity of the attack. Later he reported other evidence of a similar nature, likewise his failure to find the *Ameba coli* in other cases of intestinal disease than amebic dysentery. Amebæ have been found in the feces of individuals having various diseases, as was noted above (cholera patients), and even in the stools of normal individuals.

Osler in 1890 was the first observer in the United States to report the finding of ameba in the stools and hepatic abscess of a case of amebic dysentery. The patient came from Panama. Since then many others have reported cases of amebic dysentery occurring in the United States, among them being Musser, Dock, Councilman and Lafleur, Simon, Boston, Harris, and Stengel. Dopter reported some cases of amebic dysentery occurring in soldiers who had not been out of the country (France), the disease developing after they occupied a room inhabited shortly before by infected individuals.

[The writer has seen a case of a somewhat similar nature,—a young man of 23 years of age who had lived in Philadelphia all his life except for a brief stay in one of the New England States. He resided in Philadelphia with a young man who had contracted amebic dysentery in the Philippines, and who had been successfully operated upon for a liver abscess after an appendicostomy. I saw the patient in consultation as a case of suspected typhoid, but not being able to concur in that opinion, and finding a large liver, I suggested a dysenteric colitis and possibly a liver abscess. Some days later I saw him again, and advised an operation. This was done and the liver abscess drained. Culture made from the liver abscess was sterile, but the necrotic material contained amebæ. He gradually sank and died, as he had been ill over three months in all. W. EGBERT ROBERTSON.]

The finding of amebæ in the stools of normal individuals and of those ill with other conditions than dysentery, and the fact that rectal injections in animals sometimes failed to produce dysentery in them, led to the question whether the ameba was really pathogenetic or whether more than one variety existed, one type being pathogenic, the other benign. Several observers had already reported the finding of amebæ which were larger than that described by Lösch as the *Ameba coli,* and presenting a different encysted form. Quineke and Roos were among the first who endeavored to show that variations doubtless exist. With one type they succeeded in inducing in cats both dysentery and liver abscess, while with amebæ from another source they failed absolutely. They also described an intermediate type which caused mild intestinal symptoms when injected *per rectum* into cats. This led them to name these three as follows: *Ameba coli,* retaining the name given by Lösch to that type inducing most severe results, *Ameba coli mitis,* to the intermediate variety, and *Ameba coli vulgaris* to that type devoid of pathogenicity. These latter they obtained from the stools of normal individuals after the administration of

Carlsbad salts, finding amebæ in 9 out of 24. Schulberg also found them in the liquid stools of 10 out of 20 normal individuals after the administration of salines, but failed to find them in the solid feces. Kruse and Pasquale also found them in their own dejections and in those of many other normal individuals. Calandruccio swallowed amebæ and, though he continued to find them in his stools for some days, no morbid condition resulted. This knowledge caused Councilman and Lafleur to classify amebæ as pathogenetic and non-pathogenetic; the former they called *Ameba dysenteriæ,* the latter *Ameba coli.* The accepted classification of today, however, we owe to Schaudinn, who termed the benign type *Entameba coli,* and the pathogenetic variety *Entameba histolytica.* A third form, described by Viereck in 1907, also pathogenetic, and called by him the *Entameba tetragena,* was at first believed to be a separate and distinct entity. Craig at first subscribed to this view, as did Schaudinn, but in a recent communication ("The Identity of Entameba histolytica and Entameba tetragena," Jour. Amer. Med. Assoc., May 3, 1913) Craig states that in 3 cases of amebic dysentery from Panama and one from the Philippines he had "been able to observe every form of both histolytica and tetragena, so far as nuclear structure and reproduction goes, that have been described for either species, and, as double infection in these cases can be practically ruled out, I am forced to conclude that there is only one species of entameba present, and that all of the forms found belong to the life cycle of *Entameba histolytica.*" The fact is as Wenyon states (Jour. London School of Tropical Med., 1912, ii, part i): "The common pathogenic ameba of man is still *Entameba histolytica;* the life history is not that described by Schaudinn, but that described by Viereck." The normal method of reproduction of *Entameba histolytica* in the cystic stage of development is by the formation of cysts containing 4 daughter-nuclei according to Craig (*vide supra*), but why encystment occurs in some and not in others of the same species, and what conditions determine this, are unknown.

> *Entameba coli* is a harmless commensal in the human intestine, while *Entameba histolytica* and *Entameba tetragena* are pathogenic species, capable of producing amebic dysentery in man. *Entamebæ histolytica* and *tetragena* are strictly parasitic species and have not been cultivated. All cultivated species belong to the genus *ameba,* and differ greatly in morphology and life cycle from the parasitic amebæ which belong to the genus *entameba.* It has not been proved that any of the amebæ that have been cultivated are pathogenic to man. C. F. Craig (Amer. Jour. Med. Sci., Jan., 1913).

Musgrave is of the opinion that amebæ may become pathogenic at any time, and cites in support of this view an experience of his in Manila. Among 300 persons studied he found 101 with amebæ in their stools, of whom 61 had dysentery, the remaining 40 being symptom free. Within two months 8 of these 40 died and amebic infection of the bowel was found in all 8, and within the next three months all of the remaining 32 had dysentery.

Cultivation of the Ameba.—The importance of culturing the ameba on artificial media was early recognized. Kartulis claimed to have succeeded in inoculating non-sterilized, alkaline straw infusions from dysenteric feces and from the necrotic material of dysenteric hepatic abscesses. Incubated at 36° C. to 38° C. for about forty-eight hours, a pellicle forms on the surface, composed of amebæ and bacteria. The amebæ, at first small, gradually increase in size and assume pseudopodial progression. Kartulis described small, round, non-motile bodies within them which he regarded as spores. When sterile straw infusions were employed, Kruse and Pasquale were unable to duplicate Kartulis's work, though they succeeded with unsterilized straw infusions. Therefore they regard this particular ameba as saprophytic, which would seem to be borne out by the indifferent results following animal experimentation.

Celli and Fiocci, Beyerinck, Schardinger, Cunningham, Grassi, and others have attempted cultivation both on solid and in liquid media, but without success so far as pathogenic amebæ are concerned. It seems very probable that symbiosis with some of the bacteria is necessary for the development of pathogenic amebæ. Although Musgrave and Clegg succeeded in plating out the ameba, they were unable to demonstrate further growth and multiplication without the presence of living bacteria. This is curious in view of their presence in the bacteria-free, necrotic contents of liver abscesses; yet we know, from experimental evidence at least, that if dejections from cases of amebic dysentery be heated to 45° C. the amebæ are destroyed but no harm is done to the bacteria, and that fecal material so treated may be injected with negative result, while injections of the unheated stool give rise both to dysentery and hepatic abscess. Thus, it is evident that the bacteria alone are not responsible. No one has succeeded in producing growth and multiplication of the ameba in the absence of bacteria, and while it is not possible, at present at least, to state which germ or germs are necessary to symbiosis, saprophytic organisms, when injected with the amebæ, usually fail to give rise to disease processes, while typical results follow when pathogenic germs are simultaneously employed. After amebæ become encysted, Frosch was able to destroy the bacteria by using a 20 per cent. sodium hydroxide solution. The amebæ thus obtained in culture with the spirillum of cholera, according to Musgrave and Clegg, when injected into the liver of a monkey, gave rise to hepatic abscess in which both amebæ and cholera spirilli were found, but similar injections into a monkey immunized against cholera were without result.

[The work of Duval with leprosy may throw some light on this subject. Noting the intimate relation between cell and bacteria, he reasoned it out that the bacterial proteolysis of the cell undoubtedly set free amino-acids and that these substances were probably necessary to the growth of the organism. This he proved to be the case. A parallel state may exist in amebic infection. Saprophytes do not break down tissue; hence no result when injected with the ameba, while pathogenic germs do, thus explaining the symbiosis and resultant pathogenesis. W. EGBERT ROBERTSON.]

The pathogenicity of certain forms of amebæ, especially the *Entameba histolytica* of Schaudinn, is generally accepted for the following reasons:—

1. The more recent the attack of dysentery, the greater the number of amebæ present.

2. Their intimate relation to certain tissues, notably the colon, in which they penetrate into the deeper portions of the wall, and to the liver in abscess, in which they are to be found to the exclusion of other infective organisms.

3. The uniform anatomical picture produced as a result of their activity.

4. The similarity, to those occurring in the human, of symptoms and morbid lesions resulting from injection into the colon of experimental animals or when the infected material is fed by mouth to the animals.

Morphology.—The *Entameba histolytica* is round, oval, or sometimes pear-shaped at rest, but apt to be very irregular when actively in motion by throwing out one or more pseudopodia. It is unicellular, possessing a hyaline ectosarc which is best seen in the pseudopodia. These latter may jut out from any part of the organism and seem to drag the ameba along as the contents gradually flow into them. The endosarc is a granular inner portion and contains a rather small nucleus, poor in chromatin, and hard to recognize. There may be several nuclei and vacuoles, and erythrocytes, leucocytes, blood-pigment, bacteria, small starch grains and the like may be noted in them.

According to Chas. F. Craig, encystment only occurs under favorable conditions the nature of which are not definitely known, and quite frequently, therefore, no cysts can be demonstrated. He also states that the normal method of reproduction in the cystic stage of development is by the formation of cysts containing 4 daughter-nuclei. In the active stage it is probable that the mode of reproduction occurs by binary fission or by gemmation or budding, irregular in type. The organism varies in size within rather wide limits, from about 10 to 50 microns, the average being about 25 to 30 microns, while the nucleus is 5 or 6 microns in diameter. The *Entameba coli* is smaller, from 10 to 15 microns on an average, possessing a well-defined nucleus because it is richer in chromatin. It is less active than the *Entameba histolytica*. It is claimed by many to be a normal inhabitant of the bowel, probably the small intestine, and may be demonstrated in liquid feces after a dose of salts. It is non-pathogenic, therefore.

Modes of Infection by Entameba Histolytica.—Owing to our failure to grow amebæ in pure culture, it is not possible to isolate, from any source, an ameba of pathogenic properties answering all the conditions necessary to justify one in regarding it as the *Entameba histolytica*. We do know that both soil and water, and especially cistern or tank water, contain numerous amebæ, but even in the tropics the majority of them must be saprophytic, or amebiasis would be far more common. Drinking-water and fruits and vegetables eaten raw or only slightly cooked, and contaminated through fecal material used as fertilizer, may prove a source of infection. It is possible that the encysted form, which can withstand drying for several weeks, may be transported by air-currents and thus both food and water may become infected. The fatal case previously referred to certainly contracted the disease by contact with his brother-in-law, who resided in the same house. Many opportunities are given through various domestic utensils, toilet, or soiled hands.

MORBID ANATOMY.—*The Intestines.*—Almost any portion of the large bowel may be involved, or the entire structure may rarely be attacked. Probably the cecum and ascending colon are most frequently diseased. In the most extensive forms the entire wall of the large intestine is thickened and practically ulcerated in continuity. Occasionally the appendix is ulcerated, the cecum as a rule, and perforation of cecum or rectum is a common cause of fatal peritonitis or extensive periproctitis. The lesion is sharply delimited at the ileocecal junction. The earliest evidence of infection consists of a swelling of the submucosa, cellular proliferation and edema, local or diffuse. The mucosa over these elevated areas undergoes necrosis and sloughs, but the opening is often minute and practically always much smaller than the area of infiltration. In this stage the gelatinous submucosa constitutes the floor of an irregular ulcer with elevated, undermined edges. Soon the submucosa sloughs and is cast off as may the muscularis beneath, so that any of these structures may constitute the base depending on the stage, or the thickened serosa may remain, denuded.

> The amebæ do not make their first appearance in the submucosa. On the contrary, they are demonstrable, first in the mucosa, and make their way along the interglandular connective tissue beneath the surface epithelium. From this point of penetration the amebæ invade the glands by penetrating the basal membrane of their epithelium. Following the connective-tissue route, they arrive at the depth of the mucosa and then, after a period of delay, penetrate the muscularis mucosæ and so arrive at the submucous tissue. The first pathological effect of the presence of amebæ is an inflammatory reaction, which soon gives place to the necrotic process which is typical of their pathogenicity. Dopter (Ann. de l'Inst. Pasteur, July 25, 1905).
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> The amebæ are not in the intestinal wall in the first stage of the disease, but enter the wall after the formation of the ulcers and then aggravate the condition. The initial focus in the submucosa which penetrates into the mucosa and causes the ulceration is due to another, as yet unknown, micro-organism. Tanaka (Münch. med. Woch., Nov. 1, 1910).

Many of the ulcers will be connected by sinuous tracts covered by more or less normal mucosa. In less acute cases the ulcers are not so ragged; they are paler and the bases are often pigmented. Microscopically it will be at once noted that the process is not a purulent one, polynuclear leucocytes being almost absent. It is the fixed connective-tissue cells which proliferate and break down. The lymphatics are dilated, the blood-vessels turgid or thrombosed, the epithelial cells of the mucosa in the immediate neighborhood of an ulcer being the seat of cloudy swelling, dehiscent, the tubular glands often distorted, sometimes cystic due to pressure retention. Amebæ will be found in the bases and edges of the ulcers, out along the fistulous tracts, in the lymphatics and blood-vessels and in the tubular glands. Schaudinn believed they effect entrance to the submucosa by way of Lieberkühn's crypts. In the chronic cases all stages of the ulcerative process may be found up to areas of complete cicatrization. Coils of large and small bowel may become adherent. Stricture of the bowel with dilatation above may result in some instances.

The Liver.—It is very likely that infection takes place by way of the portal radicles, though it is difficult to explain why the hepatic lesion is large and single as a rule, rather than small and multiple as in cases of pylephlebitis. The single abscess is usually situated in the right lobe, either near the dome or less commonly beneath the undersurface, near the colon. Multiple abscesses are small, superficial, scattered throughout the outer portions of the liver, though the still smaller, miliary abscess may be widely diffused as in pylephlebitis. In addition, more or less necrosis of liver tissue may be noted focally, probably bacterial in origin. The abscesses do not contain pus, and cultures are almost uniformly sterile. The contents consist of a dirty-yellow or reddish, necrotic material, containing blood and fragments of liver tissue. The early focus is well defined, containing a spongy material with more or less dirty, blood- or bile- tinged fluid through it. Still older foci have irregular, necrotic walls or dense, reactive inflammatory walls well circumscribing them. About every necrotic focus, though less marked or absent about the rarer, very chronic abscesses, is a zone of hyperemia. Amebæ may be found in the contents of these abscesses, but as a rule they occupy a close relation to the wall, and may not appear in the drainage discharge for several days after operation.

The Lungs and Pleura.—These become involved secondarily when a liver abscess breaks through the diaphragm, an abscess of the base of the lung resulting, usually the right one, which may later rupture into the pleura, a pyopneumothorax resulting, or an empyema when the liver abscess ruptures directly into the pleura.

Rarely an abscess may rupture through the diaphragm into the pericardium, or, from the liver directly into the stomach, bowel or peritoneum, or a large vessel may be eroded.

PROGNOSIS.—Many recover under rest and appropriate treatment, but prognosis should at all times be guarded, even though the type of attack seems to be a mild one. The tendency to relapse is always present.

In Manila at the present time, if early recognized and properly treated, the patients rarely pass beyond the diarrheal stage, and many, even without treatment, never become dysenteric in the common acceptation of the term. The severe cases develop from these and from the latent ones and their characteristics are well known. Children and old people seem to manifest a decided natural immunity, but while in children the infection, when it does occur, usually is of a mild type and very amenable to treatment, the reverse is true of the aged. A striking peculiarity in both classes, as well as in Filipino natives, is the absence of liver abscess. The writer has not seen a case of this in 1000 clinical cases and 100 autopsies of natives of the Philippine Islands. The disease manifests itself in a much broader and more comprehensible clinical picture than that generally allotted to it. Waiting for actual dysenteric symptoms before making a diagnosis is responsible for a large percentage of the present mortality from this cause in Manila. Bloody stools may occur early, but usually are not seen until considerable damage has been done, and may be absent till near a fatal termination or recovery. Prompt treatment of every patient in whom motile amebæ are found, without waiting for clinical dysentery, is the safe course to follow. W. E. Musgrave (Jour. Amer. Med. Assoc., Sept. 16, 1905).

TREATMENT.—Rest in bed in all acute phases of the malady, with **liquid diet.** In all other forms, diet may be given according to the tolerance of the patient, governed of course by the severity of the intestinal symptoms. For the abdominal pain, **cataplasms** or **stupes** may prove comforting, and if tenesmus is present **starch water and laudanum** (½ pint—250 c.c.—and ½ dram—2 c.c.) or hypodermics of **morphia** are the only measures which afford relief. Bismuth preparations, salol, and the so-called intestinal antiseptics given by mouth are of no value. An occasional dose of **castor oil** or several doses of a **saline** may prove serviceable. Kartulis recommended repeated doses of **calomel**, gr. ½ to ¾ (0.03 to 0.048 Gm.) every three hours for several days, claiming that the number of amebæ were greatly reduced thereby. The danger of salivation must not be overlooked, and the fact that calomel is prone to set up a good deal of rectal tenesmus or add to the existing discomfort or actual suffering must also be borne in mind.

Report on the action of various substances on pure cultures of the *Ameba dysenteriæ*. Boric acid, eucalyptol, ichthyol, oil of cassia, and infusion of quassia have slight, if any, effect on the amebæ.

Tannic acid 1:100, **sulphate of copper** 1:2000, **permanganate of potassium** 1:4000, and **sulphate of quinine** 1:1000 have a distinct moderate deterrent effect on the growth of the amebæ and cholera spirilla within thirty minutes.

Succinic peroxide acid 1:1000, **potassium permanganate** 1:2000, **sulphate of quinine** 1:500, **nitrate of silver** 1:2000, **argyrol** 1:500, and **protargol** 1:500 exercise a very marked deterrent effect on the growth of the cultures within thirty minutes, and in the case of the silver salts and the succinic peroxide acid the action is plainly due to the destruction or inhibition of the growth of the symbiotic cholera spirillum.

Thymol, 1:2500, applied for fifteen minutes has the unique effect of destroying the amebæ, while exercising only a moderate effect on the cholera spirilla. Thomas (Jour. Amer. Med. Assoc., Jan., 1906).

Series of 542 cases in which **copper** solutions were injected. The solutions were very weak—1:10,000 to 1:8000, never stronger—used at a temperature of 106° to 109° F. (41.1° to 42.7° C.), injected far up the bowel, and retained for twenty minutes, and preceded by a preliminary warm-water injection to wash away mucus. The routine use of **magnesium sulphate** by the mouth was an adjuvant to the treatment, and the resulting stools were employed to ascertain the effect of the treatment on the number and motility of the amebæ present. A double-flow rectal irrigation-tube was employed, and the instillation of fluid was made slowly, so that no irritation of the colon was induced. Immediate benefit in subjective sensation was experienced by the patients. Pain and tenesmus vanished, stools became less frequent, blood disappeared, and the body weight increased, while the amebæ were reduced in numbers, and their motility became less marked. These results were achieved in two to three weeks. By the thirtieth day all copper-treated cases were normal, and no amebæ could be detected after magnesia purgation. By the thirty-fifth day these cases were sent to convalescent camp, and no recurrence occurred. Moülden (Med. Record, July 28, 1906).

The following method, which has given brilliant results with rarely a fatality on the Isthmus, consists in what might be called the rest supportive treatment. The patient is put to bed, absolute **rest** is enjoined, a purely **milk diet** is administered, and when great tenesmus is present **warm saline irrigations** are given two or three times daily. A preliminary dose of **castor oil** is usually advisable. The only internal medication which is given is the **subnitrate of bismuth**, which is administered in somewhat heroic doses, from a dram to a dram and a half every three hours. In the milder cases improvement begins in from three to five days; in the severer cases in from ten to fourteen days. The stools then lessen in number and become formed, and in a comparatively short time—from one to three weeks—from twelve to twenty-four hours are passed without a movement. The diet is then gradually increased and the bismuth lessened in dosage. Usually the proteids, meat and eggs, are the last to be added to the full dietary. In from one to four weeks, depending on the severity of the case, the patients are perfectly well. It is then well to give **tonics** and advise **change of air.** Deeks (Med. Record, Dec. 12, 1908).

The two procedures which should be instituted as early as possible in every case, and which undoubtedly offer the greatest measure of success are, first, the use of **ipecacuanha** by mouth, and, second, the more or less frequent administration of **enemas.** Ipecacuanha should be given in salol or keratin-coated pills to insure their passage through the stomach unsolved. Nausea and vomiting are far less liable to occur. The mode of administration is as follows: Nothing by mouth for several hours, then begin at bedtime with 1 to 1½ drams (4 to 6 Gm.) of ipecacuanha. Reduce the dose each night by 5 grains (0.3 Gm.) and continue down to a 10-grain (0.065 Gm.) dose, then repeat the procedure if amebæ are still found in the stools. Subsequently, doses of 20 to 30 grains (1.3 to 2 Gm.) should be given each night over a period of many weeks.

The use of **ipecac** in chronic amebic dysentery gave the writer remarkably good results. Experiments suggest that it had a direct destructive action on the parasite. In addition there is a chologogue and sometimes a purgative action. Clinically, in cases treated with ipecac a cessation of ameboid motion of the parasites occurs in a few hours. In one to three days they disappear completely. In the same time the stools lose their dysenteric character. Mucus and blood, later pus, disappear, and the stools resemble those of mild enteritis or even become formed. Dock (N. Y. Med. Jour., vol xc, p. 49, 1909).

Fifteen cases of amebic dysentery treated with **ipecac.** Each case had a uniform and highly favorable result. In no case was there a suggestion of a recurrence of the dysenteric attacks since the discontinuance of the ipecac. The interval elapsing in these cases varied from six months to four years. The essential points in the treatment include absolute **rest in bed** for a period of at least two weeks, a proper regulation and restriction of the **diet,** and the use of the best variety of Rio ipecac in a pill properly coated with salol [a three-hour fast preceding the administration of the pills, containing 60 grains (4 Gm.) at first, or in severe cases 100 grains (6.5 Gm.), each succeeding evening reducing the dose by 5 grains (0.3 Gm.), or 1 pill]. The employment of bowel irrigation or flushings should not be attempted during the administration of the ipecac, as it would wash the drug out of the large bowel and defeat the object of the treatment. S. K. Simon (New Orleans Med. and Surg. Jour., Nov., 1912).

Ipecac in the treatment of amebic dysentery in Florida has practically supplanted all other measures. The method employed is that suggested by Dudley, of Manila, about two years ago, and is as follows: The patient is put on a **milk diet** and confined to **bed;** after 4 P.M., takes neither food nor water for four hours, when he is given 30 grains (2 Gm.) of ipecac in six salol-coated pills, swallowing these with as little water as possible. The patient takes no food or water during the night; the next day he takes water and milk liberally until 4 o'clock, and after four hours' fast is given 25 grains (1.6 Gm.) of ipecac. The dose is reduced 5 grains (0.3 Gm.) daily until the 5-grain (0.3 Gm.) dose is reached. Patient is then put on light diet and daily dose of 5 grains (0.3 Gm.), continued for a week or ten days. If the pills are properly prepared there is little or no nausea. This treatment has given excellent results. Wallace (So. Med. Jour., Nov., 1912).

Superior even to ipecac and bidding fair to assume the position of a true specific is **emetine hydrochloride** (see the article on EMETINE, this volume) an alkaloid of ipecac recently introduced by Leonard Rogers (British Medical Journal, June 22, 1912) in the treatment of amebic dysentery and hepatitis.

Vedder had previously shown that this substance, the principal alkaloid of ipecacuanha, has the power in high dilutions of destroying amebæ in broth cultures; Rogers confirmed this by testing the effect of emetine hydrochloride on *Entameba histolytica* in dysenteric stools. When mucus containing numerous active amebæ was placed in the alkaloidal solution, the pathogenic organism was immediately killed and materially altered in its microscopic appearances by a 1:10,000 solution, while after a few minutes they were rendered inactive and apparently killed by as weak a solution as 1:100,000. Administration of emetine hydrochloride hypodermically in a few cases of amebic dysentery yielded excellent results. It did not produce vomiting, even though in the same cases ipecacuanha given by mouth had done so; the alkaloidal salt was at first given in doses of 1/6 grain (0.01 Gm.), this being equal to 15 grains (1 Gm.) of ipecacuanha. In the later cases 1/3 grain (0.02 Gm.) and even 1/2 grain (0.03 Gm.) were given without producing any ill effects on the patient, though their action on the disease was magical. The **hydrobromide of emetine** might also be given, but it is not quite so soluble as the hydrochloride. An advantage of the method is that the drug can be given even when the administration of ipecacuanha by the mouth is impracticable.

The advantages of the subcutaneous injection of **emetine** treatment are: (1) simplicity and ease of administration of the drug; (2) absence of pain, vomiting, and depression; (3) accurate dosage (no loss through the bowels); (4) rapid absorption and effect; (5) reliability of the product (hydrochloride). While the time which has elapsed is yet too short to enable one to speak with absolute certainty as to the cure, the results so far obtained are highly suggestive that we have in this an ideal method of treating amebic disease. R. Lyons (Jour. Amer. Med. Assoc., April 19, 1913).

As to enemas, they should be given slowly and as high as possible, the patient lying on the right side with hips elevated and head low; 3 quarts (liters) of a warm solution of **quinine** in strengths ranging from 1:5000 to 1:500 may be given once or twice daily, each to be retained for fifteen or twenty minutes unless the pain is too severe. An initial enema of even greater strength may be employed up to 1/2 per cent. or even 1 per cent. of quinine. It usually gives rise to buzzing, nausea, and occasionally vomiting, sweating, and a great deal of pain, but all these symptoms rapidly abate. Harris recommended **peroxide of hydrogen,** 1 to 2 pints (500 to 1000 c.c.) diluted with 4 to 8 times the amount of water. **Eucalyptol** or corresponding doses of the gum in 1 per cent. to 4 per cent. strength was advocated by Ford. Tuttle recommended simply **enemas of ice-water,** and reported a number of cases of which cures resulted from its frequent use. If definite results do not promptly follow the above measures an **appendicostomy** should be performed, and **ice-water** or **quinine lavage,** or these latter alternating with

hydrogen peroxide or **eucalyptol,** should be introduced through the appendicostomy opening and the bowel thoroughly irrigated twice daily.

As soon as a diagnosis of liver abscess has been made, it should be opened and drained and the cavity thoroughly washed out with **quinine** solution.

> The writer treated chronic dysentery by **irrigation of the colon** through the vermiform appendix or an opening into the cecum in 6 cases, and is very favorably impressed with the results, although the number is too small to enable definite conclusions to be drawn. The advantages of this method of irrigation over the deep rectal injections are: (1) The irrigating fluid is delivered first at the point shown by experience at the post-mortem table to be the location of the most extensive lesions, and is carried from there by the natural peristaltic movement of the colon to the outlet. Rectal irrigations, to reach even the transverse colon, must overcome this natural tendency of the bowel to drive out any foreign substance. (2) It is entirely painless, and very much easier for the nurse to administer. Indeed, the patient can soon be taught to do the irrigating himself. (3) It is possible to keep it up much longer, for rectal irrigations soon become so distressing that they must be discontinued for long periods. W. H. Arthur (Med. Rec., March 25, 1905).
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> The writer advocates surgical treatment in all cases of amebic dysentery when amebæ persist in the stools after one year's patient trial of irrigation through the rectum and the amebic ulceration is higher up in the intestine than the sigmoid flexure. The preferable operation is **appendicostomy.** Holt (N. Y. Med. Jour., Nov. 16, 1907).
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> **Appendicostomy** is indicated when the case is refractory to rectal irrigations. The writer met with marked success in 2 cases, using **quinine** or **saline solution** through fistula. The operation should be performed in two stages: first bring base of appendix against abdominal wall, stitching mesoappendix to peritoneum; forty-eight hours later, apply cocaine to appendix, snip off with scissors, and introduce No. 10 rubber catheter. Anders and Rodman (Jour. Amer. Med. Assoc., Feb. 12, 1910).
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> Four cases of **appendicostomy** for dysentery, 2 of amebic and 2 of bacterial character, in all of which marked improvement or a cure resulted. Appendicostomy is less dangerous and more reliable even than high irrigation in cases of ulceration of the bowel. The writer prefers a transverse to a lateral one along the sheath of the rectus. To insure success it is necessary that the appendix should be sufficiently long and movable, though adhesions may be separated and the mesenteriolum detached to enable the appendix to be sutured in position without undue traction. It is important, however, to avoid separating the entire mesentery, as this might lead to gangrene of the stump. O. Müller (Münch. med. Woch., Nu. 41, 1912).

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DYSMENORRHEA. — DEFINITION.—Dysmenorrhea is not a disease, only a symptom. The term has often been used in a very loose way to signify any or all the painful or other disagreeable sensations which may be associated with the abnormal performance of the function of menstruation. The headaches, the pains in the joints and muscles, the backaches, the nausea and vomiting which are of such frequent occurrence at the menstrual epoch do not constitute dysmenorrhea, though they are doubtless influenced by the same cause which produces dysmenorrhea. This symptom must be referred to the pelvic organs, to their nervous system, and to their vascular system; in other words, dysmenorrhea is pain in the pelvic organs which is experienced in connection with the function of menstruation. It is a symptom of a pathological condition. A woman who is in perfect physical condition menstruates without pain.

Dysmenorrhea may, therefore, be defined as a deviation from normal menstruation, menstruation meaning essentially a monthly congestion of the vascular system of the pelvis in obedience to a recurring impulse, with the shedding of more or less of the endometrium and the discharge of glandular secretions, the tension of the vascular system being relieved by the discharge through the uterine canal of a greater or smaller quantity of blood.

SYMPTOMS.—The pain of dysmenorrhea differs as to the time of its occurrence, its intensity, its duration, and the conditions which produce it. It occurs most frequently during the day or the two or three days which precede the menstrual flow.

> Report of 20 cases of intermenstrual pain besides 25 collected from literature. The pain generally occurred from twelve to sixteen days after the beginning of the previous menstruation and continued from two to four days, reached its maximum on the first or second day, was often different in character from the menstrual pain, and was rarely accompanied by discharge. Attributed to awakening of menstrual activity for the coming menstrual period. Malcolm Storer (Boston Med. and Surg. Jour., April 19, 1900).

In many women the beginning of the flow means the relief of tension and the relief also of pain; with others it continues, sometimes diminishing, sometimes retaining its acuteness until the pelvic congestion has subsided.

The pain may be a simple ache, a feeling of distention within the pelvis, or it may be an acute, continuous, neuralgia-like sensation. It is often spasmodic in character, with a feeling of contraction or bearing down in the uterus, and may be relieved when a clot or gush of blood is ejected from the uterine cavity. The acuteness of the pain also depends upon the temperament of the patient, a highly organized sensitive person suffering more than a phlegmatic, insensitive one. It is more frequently experienced in damp than in dry weather, at the seashore rather than at the mountains, during an ocean voyage rather than on a journey inland. The more scar-tissue there is in and around the uterus, the greater the flexion of the organ, and the narrower the cervical canal, usually the more constant will be the occurrence of pain.

The customary classifications which can be verified by anyone with a few years of practical experience are, for the most part, satisfactory, but the writer has adopted the following as the results of his experience, viz.:—

1. Dysmenorrhea from congestion.
2. Dysmenorrhea from obstruction.
3. Dysmenorrhea from neuroses.
4. Dysmenorrhea from endometrial hypertrophy.

1. Dysmenorrhea from congestion. This is the simplest of all the varieties. Congestion is always and necessarily a feature of menstruation; that is, the current in the pelvic vessels is then more rapid, or the tension or volume is greater, or, perhaps, all these elements are combined. When the degree of this congestion is greater than can be readily tolerated by the person, pain is one of its results (the other results need not concern us now), and this pain will last as long as the congestion continues, and will recur as frequently. Tolerance of

this condition to a greater or lesser extent is acquired by many women, just as other disagreeable experiences become tolerable when habitual and inevitable. In some cases the pain seems limited to one or both ovaries, in others to the uterus, and in others it seems to be distributed through the pelvis.

> Menstruation as the abortion of an unfertilized ovum; ovulation should naturally be followed by impregnation, but as it does not every time in the human race the various phenomena of ovulation must be conquered, which adaptation is outwardly shown by the function of menstruation. A nervous individual may react abnormally to the impulses of ovulation; in her the phenomena of conquering such impulses may not occur and the result is one of the forms of nervous dysmenorrhea. Another form is due to the faulty development of the uterus with co-existent abundant sexual excitement; the latter leads to changes in the ovaries and in the endometrium and to the symptom of dysmenorrhea, which in this case depends upon both anatomical and functional disturbances. The third form is the purely mechanical one due to some local disease or anomaly of the uterus or of the neighboring organs. Veit (Münch. med. Woch., Nov. 24, 1908).

> Dysmenorrhea is frequent in young nulliparæ without gross pathological lesions. Its most frequent cause is hypoplasia of uterus or ovaries or a pathological anomaly preventing expulsion of the menstrual products. The seat of the cause of dysmenorrhea is rarely in the cervix. Pathological anteflexion rarely causes it. The cause must be carefully studied. Norris and Barnard (Amer. Jour. of Obstet., May, 1910).

2. Dysmenorrhea from obstruction. There has been much discussion for many years concerning this variety, some writers going as far as to say that the vascular system of the pelvis was so accommodative that dysmenorrhea from obstruction was not possible. Clinical facts do not warrant such a statement. Obstruction of the outflow of blood is, perhaps, not so great when the womb is flexed backward or forward as was claimed a few years ago by Sims, Hewitt, and others, especially if coagulation of the blood within the uterus does not occur; but if such coagulation does take place (and in some cases also in which it does not), dysmenorrhea will be a very pronounced symptom.

With stenosis of the cervical canal the same difficulty to the outflow of the menstrual product is also frequently observed. With imperforation of the hymen or of the os internum or externum obstruction to outflow is complete. A certain portion of the transuded blood is reabsorbed, but the remainder persists, distending the vagina or the uterus or both, sometimes producing a very large tumor, and invariably resulting in great pain, which in some cases has led to a fatal result.

> Small fibroids found to be the cause of dysmenorrhea in 3 cases in spinsters aged about 32 years. In 2 of the cases the uterus was removed; in 1 of these a small interstitial fibroid, about 7 mm. in diameter, was found in the isthmus; in the other, two similar small nodules wer found in the same situation. In the third case a vaginal celiotomy was performed, and the presence of an interstitial fibroid about the size of a hazelnut at the level of the isthmus recognized. This was removed by simple enucleation. All the cases were cured of their symptoms. Wilson (Brit. Med. Jour., No. 2651, p. 996, 1911).

Pain from incomplete development of the pelvic organs, especially the uterus, is also to be referred to obstructive dysmenorrhea as its origin, and, as in certain cases of congestive dysmenorrhea, the bad symptoms are not limited to pain. Dysmenorrhea from inflammatory exudate is an acquired symptom, the exudate binding the pelvic organs into a more or less firm mass, which tends to become firmer as the contraction, which time brings with it, takes place. The pain in such cases is not limited to obstruction to outflow; indeed, there is no such obstruction apparent in some of the cases, the flow being profuse in some instances and scanty or absent in others. The remarks concerning inflammatory exudate will also apply to scar-tissue, which, by its presence, will often effectually obstruct the passage of the menstrual blood-current. To this variety of dysmenorrhea might also be added those cases, which are so often seen, that depend upon perverted or imperfect nutrition and in which constipation is an ever-present accompanying symptom.

3. Dysmenorrhea from neuroses. There may be at least two types of this variety; in one of them the neurosis is the sole discoverable source of trouble; in the other it is secondary to disease of some other character within the pelvis.

> In many cases of painful menstruation, the dysmenorrhea is not due to minor palpable changes in the uterus or ovaries. This is shown by the fact that they are not permanently relieved by operation. Such cases belong, therefore, to the neurologist rather than to the gynecologist. Hence the propriety of careful observation of the patient, a guarded prognosis, and less frequent resort to operation before fair trial has been made of local and general measures. Coe (Amer. Jour. of Obstet., May, 1911).

Hysteria is at the foundation of many of the cases of the first-mentioned variety, the pain connected with menstruation being, to a great extent, simulated or imagined.

When we realize, however, the intimate anatomical relations which the sympathetic nerves of the pelvic organs bear to the nerves and ganglia of the rest of the organs of the body, we are quite prepared to believe that painful sensations in these organs might be transmitted to the organs of the pelvis. So far as I know, there have been no exact investigations upon this subject. The referred or reflected pains from the pelvic to the other organs have been much discussed and a variety of conclusions has been reached. The neuroses in the pelvis or pelvic organs which occasion dysmenorrhea may constitute a use of language which is somewhat misleading. Of course, all pain is the evidence of nerve irritation or a neurosis. The form which is here to be considered is that in which, aside from mere congestion or obstruction as an attendant of the menstrual experience, there is a direct irritation of nerve-tissue which is not apparent apart from the menstrual epoch. Such, for example, is the case when the unusual pressure due to the congestion of menstruation is experienced by the sacral nerves as they pass through the pelvis, the tissues being already the seat of inflammatory exudate. The tissues are squeezed and contracted by this exudate; but the addition of the menstrual congestion introduces a further element of pressure, which causes irritation of the nerves which are impinged upon, and pain is experienced, which radiates in the direction of the imprisoned nerves. This condition is not infrequently found in insane women; it is probably a factor in producing insanity, and such insanity cannot be expected to ameliorate permanently until the source of trouble is removed.

> Eisenstein found that 118 women with menstrual disturbances gave a positive

> reaction to a subcutaneous injection of tuberculin, although there was nothing else to suggest tuberculosis. The writer found in 3 cases tuberculous lesions at autopsy of young women who had been treated for dysmenorrhea. In another case of the kind the severe abdominal pain compelled laparotomy, which revealed advanced tuberculous lesions in the pelvic organs. Pfannenstiel has reported a case in which rapid miliary tuberculosis in the abdomen followed laminaria dilatation of the cervix done for dysmenorrhea; the patient was an apparently healthy young woman. The writer obtained a positive response to the tuberculin test in 21 of 30 patients who had applied for relief from primary dysmenorrhea. The response was always negative in the cases of secondary dysmenorrhea. With the primary form the genitalia are always defectively developed. In 11 cases there was also a local reaction in the genitalia. These findings suggest that the defective development of the genital organs was the consequence of some tuberculous process in the pelvic organs during childhood, this process possibly healing. Gräfenberg (Münch. med. Woch., March 8, 1910).

4. Dysmenorrhœa membranosa. This is a somewhat rare form of dysmenorrhea, but one which has long been recognized, and is described by all writers of gynecological treatises.

Dysmenorrhœa membranosa is due to an hypertrophied condition of the endometrial decidua; that is, of the exfoliative portion of the uterine mucous membrane which is shed at each menstrual epoch. This membrane varies in thickness and density, in extreme instances showing a perfect cast of the cavity of the uterus.

Separation of the membrane from its underlying attachment and its expulsion from the uterus mean an unusual amount of uterine work and severe pain as an almost constant accompaniment. It usually occurs, too, in women whose nutrition is defective, and is consequently a matter of more serious importance than if it were among the robust and well nourished. It is, of course, a form of obstructive dysmenorrhea, but its peculiarities are so marked that it may be well to continue to consider it a distinct variety.

ETIOLOGY AND PATHOLOGY.—Anything which prevents or disturbs the equilibrium of the normal conditions described will cause dysmenorrhea. It is of exceedingly frequent occurrence. It is a matter of great surprise that so many women should present this symptom, which appears with some of them at the advent of puberty and continues with varying intensity until the termination of menstrual life, while with others it disappears with pregnancy, with the physical changes attending mature life, or as the result of surgical treatment.

That it should occur so frequently, and especially in communities in which the highest intellectual development has been reached, is not a flattering commentary upon the results of modern civilization. Still, this is counterbalanced by the fact that dysmenorrhea is usually curable by judicious means.

> A thorough revision of our views on this subject has become necessary in the light of recent experience. More than 75 per cent. of the cases of painful menstruation are not dependent upon anatomical causes. The pain is really due to tetanic contraction of the circular muscle at the os internum, such as occurs in other sphincter muscles in neurotic subjects. Menge's theory that dysmenorrhea is due simply to an exaggeration of the contractions of the longitudinal muscular fibers, which always accompany normal menstruation, does not hold, for, if the symptoms were due purely to mechanical obstruction, it should invariably disappear after

childbirth, which is not the case in nervous and hysterical women. Uterine colic cannot be due only to the passage of clots, since in many typical cases of dysmenorrhea there is a free escape of fluid blood. Moreover, the pains are often most severe from twelve to twenty-four hours before the flow appears, instead of on the second or third day, when it is most profuse and clots usually appear. Theilhaber (Centralb. f. Gynäk., No. 3, 1902).

Dysmenorrhea is seemingly on the increase and is developed in proportion to the strenuousness of the human existence. The period of puberty should claim the attention of the physician as a promising field for preventive gynecology, as it is at this impressionable period that the foundation for future suffering is laid. It is the duty of medical men to urge the necessity of properly caring for the physical side of the schoolgirl, not permitting the mental faculties to be trained at the expense of the physical side.

While mindful of the great value of surgery in the treatment of certain well-defined pathological conditions in the pelvis, there is a growing tendency to abuse its application in reference to dysmenorrhea, and as a whole the results obtained through its intervention are nothing of which we can be proud.

A more careful study in analysis of these cases with especial reference to the etiological facts should be made, with especial reference to the value of the application of the general hygienic laws, electricity, massage, exercise, etc., in contradistinction to the reckless and loose surgical measures resorted to in their treatment. Dilatation and curetting are of value in well-defined cases, but as a routine procedure are woefully abused. In the light of recent experience obstructive dysmenorrhea is rare, and the mechanical side of dysmenorrhea is not looked upon as an etiological factor with the same degree of frequency now as in the past.

There is a close dual relationship existing between the generative organs and the general health, and in the treatment of dysmenorrhea it should be constantly remembered. S. M. D. Clark (New Orleans Med. and Surg. Jour., August, 1904).

Dysmenorrhea accompanied by labor-like pain is often due to a form of membranous dysmenorrhea, and the shreds of tissue passed are often extremely small. A histological study of the shreds show an inflammation present, even though no evidence of infection can be noted in the case clinically. The passage of shreds, if the cervix is a multiparous one, is not necessarily accompanied by pain. The writer has attained best results from **dilatation** and **curettage,** followed by the insertion of a **Wylie drain,** together with tonics and improved hygiene, and under this treatment sterility may often be overcome. C. C. Norris (Univ. of Penna. Med. Bull., June, 1908).

Women in the savage or barbarous state and women who are constantly engaged in out-of-door labor are seldom sufferers from this cause, though their pelvic organs may be defective in structure, and though they may habitually be subject to experiences which would unfailingly cause dysmenorrhea or even complete suppression of the menstrual function in women of less robust organization. This is, in part, owing to the increased power of resistance to physical ills which is favored by an out-of-door life, and, in part, to the greater insensitiveness to pain of women in the lower strata of social and intellectual development.

With those who are sufferers the underlying causes are various, and demonstrate the important rôle which the reproductive organs play not alone in the propagation of species, but in the experiences of daily life.

One hundred and twelve cases of dysmenorrhea examined. One of the most striking points is the very large number of sterile women; 44, or a fraction less than 40 per cent., belong to this

> class. Of those who had been pregnant, 12 had never had a child at full term; 15 more had had a miscarriage since the last full-term child was born, leaving less than 37 per cent. of the total number whose last pregnancy had come to full term. These figures would seem to indicate that, in a large proportion of patients suffering from dysmenorrhea, there were present lesions which also interfered with conception. One hundred out of the 112 suffering from painful menstruation were found to have some marked organic lesion of the pelvic organs. William S. Gardner (Atlanta Med. and Surg. Jour., Dec., 1895).

The causes may be classified as follows, viz.: heredity, disease, occupation, and trauma.

1. Heredity. With many women the defects in the structure of the reproductive organs are congenital and necessitate dysmenorrhea.

> Inflammatory diseases of the ovaries and the Fallopian tubes and adhesive deformities of the uterus are at times the causes of dysmenorrhea. In 100 of Kelly's operations on tubes and ovaries the appendix was found adherent in 21 cases, and in 7 it required removal. Out of 58 personal cases in which inflammatory appendages had to be removed, the appendix showed enough evidence of disease to justify removal in 20 cases. In 9 of these the adhesions between the appendix and the right appendage were very intimate. A. MacLaren (Amer. Gynec. and Obstet. Jour., July, 1900).

It does not avail that the remainder of the physical organization is normally developed; indeed, one frequently sees women of the finest physique and superb presence whose incomplete pelvic apparatus condemns them to semi-invalidism during a considerable portion of each month.

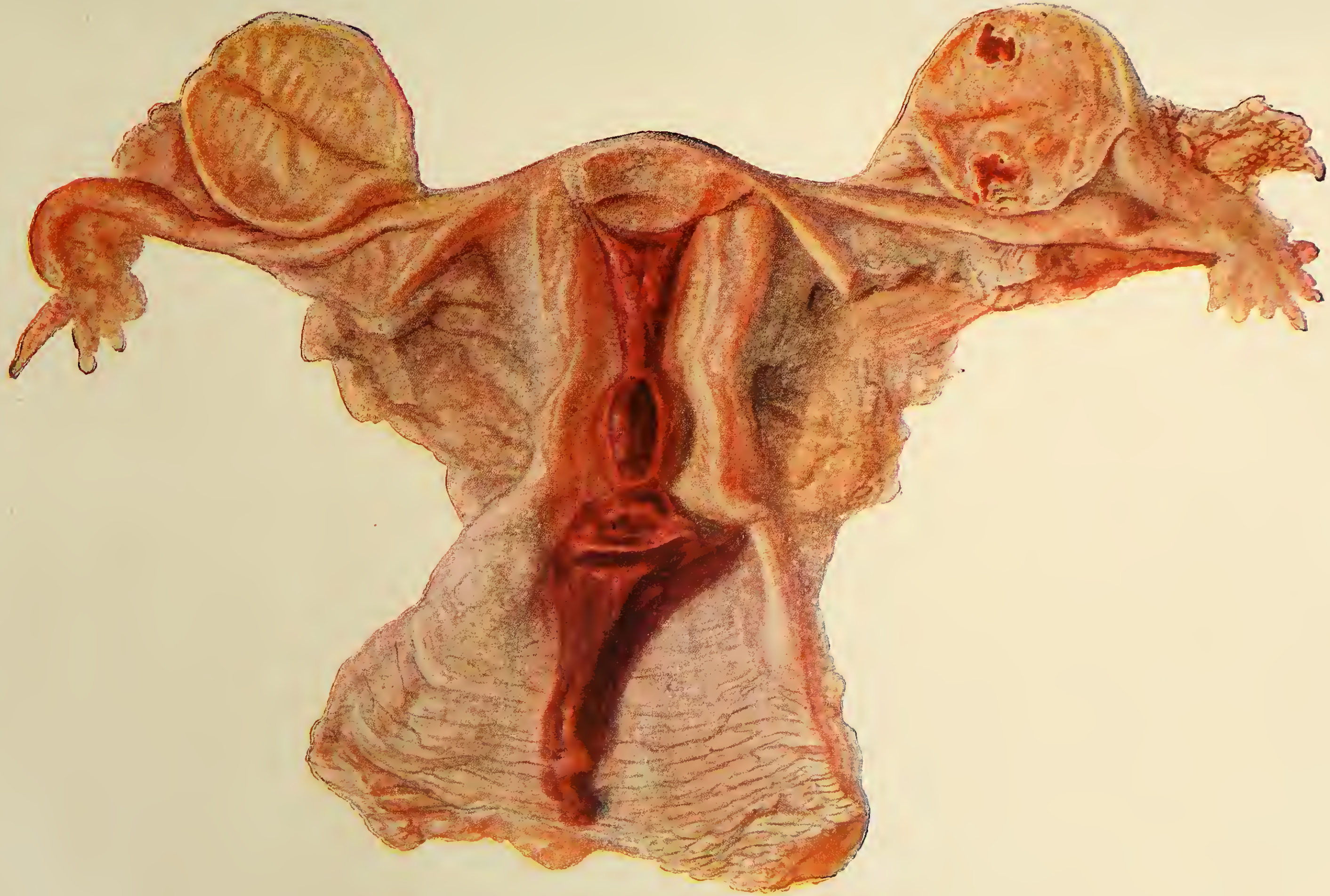
On the other hand, puny, delicate women with normally developed pelvic organs suffer with dysmenorrhea on account of their perverted general nutrition, their flabby muscular system, and their low-ebb vitality, to which the recurring monthly congestion brings a strain which they are ill fitted to bear.

The defective organization may include any portion of the genital apparatus; in the vulva it may take the form of an impermeable hymen, producing an absolute barrier to the discharge of imprisoned blood; in the vagina it may consist of bands and septa with almost equal obstruction to the outflow of the menstrual fluid; in the uterus it may be an almost impervious cervical canal, an occluded os internum or externum, less frequently a rudimentary corpus uteri or one with its two halves uncoalesced or its canal obliterated; in the tubes or ovaries the structure may be rudimentary or the seat of some form of congenital disease.

> Membranous dysmenorrhea has no connection with pregnancy or abortion, is not productive of sterility, and can become cured spontaneously. The fibrinous membranes are to be regarded as true dysmenorrheic membranes, and are not dependent upon an inflammation of the uterine mucosa. Fibrinous membranes are the product of necrosis originating in hemorrhage and transudation. Kollmann (Wiener klin. Rund., April 29, 1900).

In all cases thus connected with heredity, defective organization, etc., recurring monthly congestion produces tension in poorly conditioned structures, and, if the tension in the vessels is sufficient to result in transudation of their contents, the outlet being imperfect or wanting, pain will be the inevitable result.

2. Disease. Disease of one kind or another may cause dysmenorrhea, whether the disease occurs before or after puberty. Before puberty there are many forms of disease which arrest the development of the pelvic organs and re-



Menstruating Uterus, Showing Corpus Rubrum in Left Ovary.

sult in dysmenorrhea. The exanthemata seem to be especially productive of this effect. Why this should follow has not been satisfactorily explained. Measles, scarlet fever, small-pox, all have their victims in whom such a result has been observed.

Of the diseases subsequent to puberty which produce dysmenorrhea there are those which are local and others which are general. Of the former may be mentioned fibroid tumors, either within the uterine canal, in its muscular substance, or within its peritoneum, and inflammatory disease of the tubes, of the ovaries, or of the pelvic peritoneum. All these diseases may, by their obstructive effect, prevent free discharge of blood during the menstrual epoch, and produce pain. Of the general diseases may be mentioned typhoid fever, certain diseases of the liver and gall-bladder, anemia, etc.

The same result is often seen in cases in which there is excessive development of fat. Women who become very obese are very frequently sufferers from dysmenorrhea.

3. Occupation. Some occupations are especially prone to result in dysmenorrhea. Those who work in a very hot atmosphere, like cooks and laundresses; those who are constantly exposed to cold and dampness, like fishwives or workers in mines (unwomanly occupations); those who work in poisonous substances,—copper, arsenic, lead, phosphorus, and sulphur; those who are confined for long hours in factories, stores, and tenement-house "sweat-shops" are, in many instances, sufferers with dysmenorrhea.

4. Trauma. Dysmenorrhea from this cause is, in most cases, the result of difficult parturition, the genital organs sustaining severe injuries and cicatrization and contraction ensuing. The hardened tissues are anemic, and the necessary elimination of blood is accomplished with difficulty and pain. Occasionally there are direct injuries to the genital organs, apart from parturition, which also produce deterioration of the tissues of those organs, and are likewise followed by painful menstruation.

PROGNOSIS.—The prognosis in dysmenorrhea varies with the conditions and varies also with the treatment. If it depends upon structural defects, and those defects are remediable, a cure will result. It sometimes persists during the whole menstrual life, but with many women it gradually becomes tolerable, as all ills which are long endured become tolerable.

With regard to prognosis much will depend upon the general condition of the subject, great improvement in that direction often leading to menstruation, which is less painful or not painful at all. The prognosis in cases in which drug treatment alone is used is very uncertain; while such treatment is proper enough simply as a means of relieving or benumbing pain, it has nothing more than a temporary and palliative effect when the pain is due to an anatomical fault or defect.

> Successful treatment demands painstaking efforts to identify the underlying cause. The purely congestive type is not relieved by operation. General treatment may give relief, but at best the prognosis is unfavorable. The prognosis must be guarded when the congestive and expulsive types are combined. The expulsive or obstructive type yields readily to operation. Norris and Barnard (Amer. Jour. of Obstet., vol. lxi, p. 753, 1910).

TREATMENT.—It might be quite apparent from the foregoing that, while the treatment may be either medical or surgical, the latter, however, will usually give the more satisfactory and radical results. Modern gynecology is cast in surgical lines, and, while it would be folly to deny that many mistakes have been made in its name (for mistakes are always made in the development of a new department of knowledge), it has approached nearer to fundamental conditions by directly attacking tissues which are involved in disease than have other methods of treatment which are more circuitous in their course.

Considering the subject of treatment, therefore, as divisible into palliative and radical, the former will include the methods by means of drugs (which occasionally may produce a permanent result), and the latter (which do not infallibly produce a cure) those methods which involve surgical procedures. Of caurse, a judicious combination of both medical and surgical means will often prove efficacious.

Of the drugs which may be given to relieve the pain of menstruation, **morphine combined with atropine** should be reserved for very rare cases, whether given by the mouth or hypodermically. It should be given in the smallest possible doses, 1/8 grain (0.008 Gm.) sufficing to relieve pain in most cases as well as a larger quantity. One must not forget the seductive influence of this drug, especially upon real nervous, hysterical women. Many women find relief from the pain in question by drinking hot herb-teas: **chamomile, scutellarium, boneset, flaxseed**, etc. These can do no harm as to the formation of drug habits.

The writer found the following treatment uniformly successful for the relief of pain. He injects 1/60 grain (0.001 Gm.) of **atropine** dissolved in a cubic centimeter (16 minims) of water into the cervix, and then introduces a dry tampon. If no instruments are at hand, a small cotton tampon moistened with a 1 per cent. solution of atropine and introduced to the posterior fornix is equally effective. Drenkhahn (Zentralbl. f. Gynäk., Nov. 19, 1910).

In dysmenorrhea, if the pain is not very severe the writer gives the following:—

℞ *Potassium bromide.*	♏xv (1 c.c.).
Potassium bicarbonate	gr. xv (1 Gm.).
Sweet spirit of niter.	♏xxx (2 c.c.).
Tinct. of capsicum.	♏iss (0.09 c.c.).
Compound tinct. of chloroform (Brit. Pharm. Codex)..	♏x (0.6 c.c.).
Syrup of ginger...	♏v (0.3 c.c.).
Peppermint water, enough to make..	℥j (30 c.c.).

M. Sig.: This dose to be taken every three hours. Blacker (Pract., Oct., 1911).

The writer recommends, for allaying the pains before the crisis, prolonged **hot baths** (98° to 104° F.—36.7° to 40° C.), once, twice, or even three times daily. As soon as the crisis comes on the use of the following liniment has been found of great value:—

℞ *Essential oil of chamomile,*	
Essential oil of hyoscyamus	āā ʒss (2 c.c.).
Tincture of opium ...	ʒx (40 c.c.).
Chloroform	℥iss (45 c.c.).

Or small enemata of boiled water at 122° F., to which are added from 20 to 30 drops of:—

℞ *Tinct. of belladonna,*	
Tincture of cannabis indica	āā ʒss (2 Gm.).
Tincture of opium..	ʒiiss (10 Gm.).

M.

Suppositories may be used in place of the enemata, as:—

℞ *Morphine hydrochloride*	gr. 1/3 (0.021 Gm.).
Extract of belladonna,	
Extract of cannabis indica	āā gr. 1/6 (0.01 Gm.).
Antipyrin	gr. viij (0.5 Gm.).
Oil of theobroma.	gr. xlv (3 c.c.).

In nervous dysmenorrhea general treatment is advised and the use of the following pill:—

℞ *Extract of belladonna* .... gr. ⅙ (0.01 Gm.).
Extract of hyoscyamus .... gr. ⅓ (0.02 Gm.).
Zinc valerate .... gr. j (0.065 Gm.).
M. Fiat pilula.
S.: Three or four to be taken each day.

Or, one tablespoonful of the following may be given, from three to five times a day:—

℞ *Solution of ammonium acetate*...... ʒj (4 c.c.).
Syrup of saffron.... ℥j (30 c.c.).
Infusion of bitter orange-peel .... ℥iss (45 c.c.).
Infusion of melissa q. s. ad .... ℥vj (180 c.c.).
M.

Or, every half-hour one tablespoonful of

℞ *Syrup of opium,*
Solution of ammonium acetate,
Syrup of bitter orange flowers ....āā ℥ss (15 c.c.).
Elder-flower water.ad ℥vj (180 c.c.).
M.

Siredey (Paris méd.; N. Y. Med. Jour., Dec. 16, 1911).

Dysmenorrhea in many cases may be the result of spasmodic contraction of the uterus from abnormal irritability of the sympathetic-nerve terminals in the uterus, the result being an abnormal exaggeration of the automatic movements of the uterus. This "cramp theory" harmonizes best to date with clinical experiences, and treatment on this basis is giving surprisingly favorable results. In the 5 cases reported he prescribed two or three 0.0005-Gm. (1/120 grain) pills of **atropine,** commencing a few hours before the anticipated onset of the dysmenorrhea. Although slight dryness of the throat occurred, the patients were relieved of all tendency to dysmenorrhea. Novak (Zentralbl. f. Gynäk., April 15, 1911).

More or less meritorious preparations are much in vogue, but in some cases they seem to be entirely inert, either from instability or want of uniformity in the preparation or some peculiarity in the patient.

Manganese is a most valuable remedy in unmarried women, and a trial extending over three months is recommended before relinquishing its use. Its action appears to be upon the nerves or nerve-centers concerned in the menstrual function rather than upon the blood. Administration of manganese does not interfere in any way with **iron** and vegetable tonics, but rather enhances their effects. The **black oxide** is the most convenient form of prescription. If nausea is produced the drug should be given in a small dose: 1 grain at a time gradually increased. A 3-grain (0.2 Gm.) dose is found to be as efficacious as a larger one. Charles O'Donovan (Med. News, Nov. 27, 1897).

The following formula has given good results:—

℞ *Tincture of hydrastis Canadensis,*
Tincture of viburnum prunifolium,
of each, equal parts.

M. Sig.: Ten drops to be taken every two hours. Lutaud (Jour. de méd. de Paris, Jan. 2, 1898).

In cases in which the flow is ushered in by severe cramp-like pains for three or four days preceding the menstruation, ½-dram (2 c.c.) doses of the fluidextract of **viburnum prunifolium** in hot water three times a day may be given, and on the morning of the expected period a a full dose of **magnesium sulphate.** If the pain comes on in spite of this, 5-grain (0.3 Gm.) doses of **antipyrin,** repeated every two hours for three doses, if necessary, will often relieve it. Arthur A. Browne (Montreal Med. Jour., April, 1898).

In dysmenorrhea **thyroidin** is "a uterine and ovarian anodyne and sedative, as it arrests the different impressions at their formation." One grain (0.065 Gm.) of thyroidin is given in capsules thrice daily for two days before menstruation is due; the quantity is increased to 2 grains (0.13 Gm.)

thrice daily during the flow. Relief is afforded in over 80 per cent. of cases. The treatment is efficient when the uterus and ovaries are in normal position. Any pathological lesion must be remedied by proper surgical measures. Stimson (Amer. Jour. of Obstetrics, July, 1902).

Ovarian extract is indicated wherever there is deficient function of the ovaries. The proper dose is 2 tablets daily (1 after the middle meal and 1 after the evening meal). Usually the administration of 200 tablets, repeated three times, is sufficient to correct any disturbances resulting from disturbed ovarian function. In castrated women, on the other hand, the preparation must be given constantly or at least until the body has accustomed itself to the precocious climacterium, since the organism is no longer able to elaborate the necessary hormone.

Iron should be added to the ovarian extract, since most patients suffering from hypofunction of the ovaries are also anemic. On the other hand, it must be remembered that chlorosis has recently been attributed to deficiency on the part of the ovaries. C. Lau (Med. Blätter, Nu. 17, 1912).

In many cases of deficiency of ovarian function in young women there are digestive and nervous signs which suggest actual and relative hyperthyroidism. It is important, in the many instances where trouble occurs in association with menstruation—usually in the premenstrual phase, to distinguish between cases due to excess of the ovarian secretion itself and those in which there is hyperthyroidism due to deficiency of the antagonistic ovarian function.

The distinction between these two conditions can often readily be made by the use of **thyroid substance,** the latter variety of cases being made distinctly worse by the drug in doses of 1 to 5 grains (0.065 to 0.3 Gm.) three times a day, while the former class is benefited by the thyroid substance. Where the ovarian function is deficient, **ovarian substance** is very effective. S. W. Bandler (Archives of Diag., Jan., 1913).

The various currents of **electricity** have all been vaunted as useful means of treatment, and in many cases they are prompt in producing relief. Especially is this true of the **faradic current,** but if the cause of the trouble lies in a defect of structure it would be unreasonable to expect a permanent result from electrical treatment so long as the cause remains.

Other palliative measures are **warm hip-baths** in which the patient may sit ten to fifteen minutes, the temperature of the water being sufficient to produce relaxation of tissue, and **hot mustard-water foot-baths,** which must be used only long enough to produce a glow of the skin. **Hot salt baths** calm the pains of dysmenorrhea and notably diminish menstrual flow, according to Mironoff. Mundé found, in cases in which menstruation was not profuse, that the mother-tincture of **pulsatilla** in 5-drop doses every three hours was very useful.

With **mud-baths** and the **medicated waters of Kreuznach, Aix, Toplitz, Schwalbach,** and other well-known European resorts useful results have been obtained, but they are not available for the majority of our American patients.

A **change of residence,** especially from the seashore or near the sea-level to an elevation of 1000 or 2000 feet, will often give permanent relief. The writer has repeatedly seen women who menstruate with great discomfort at the seashore, while on sea voyages, or in a damp atmosphere under some other conditions. Of course, if there is no anatomical lesion one usually becomes habituated to atmospheric conditions after a few months or years.

If the pain is due to a neurosis the

treatment should be addressed to the nervous system,—the **bromides, hyoscyamus, aconite,** and the **coal-tar preparations** being employed.

If the general nutrition is at fault it is hardly necessary to say that it should be improved by a carefully selected **diet,** suitable **exercise,** cheerful companionship, and always, and above all, by the use of approved **laxatives** to keep the bowels freely open. Again and again has the writer found a constipated habit at the bottom of a history of painful menstruation.

The only cure other than by medical treatment is **childbearing.** Although the co-ordination of the menstrual and sexual function are both imperfect, and consequently the meeting *in utero* of the germ cell and the sperm cell is not helped as it should be; yet, nevertheless, the germ cell and the sperm cell may meet, and pregnancy occur; and then, in most such cases, dysmenorrhea is cured. E. Herman (Brit. Med. Jour., April 17, 1909).

If admitting the explanation of Shultz as to the cause of pain, that such uteri are hypoplastic, there is a predominance of connective tissue and a

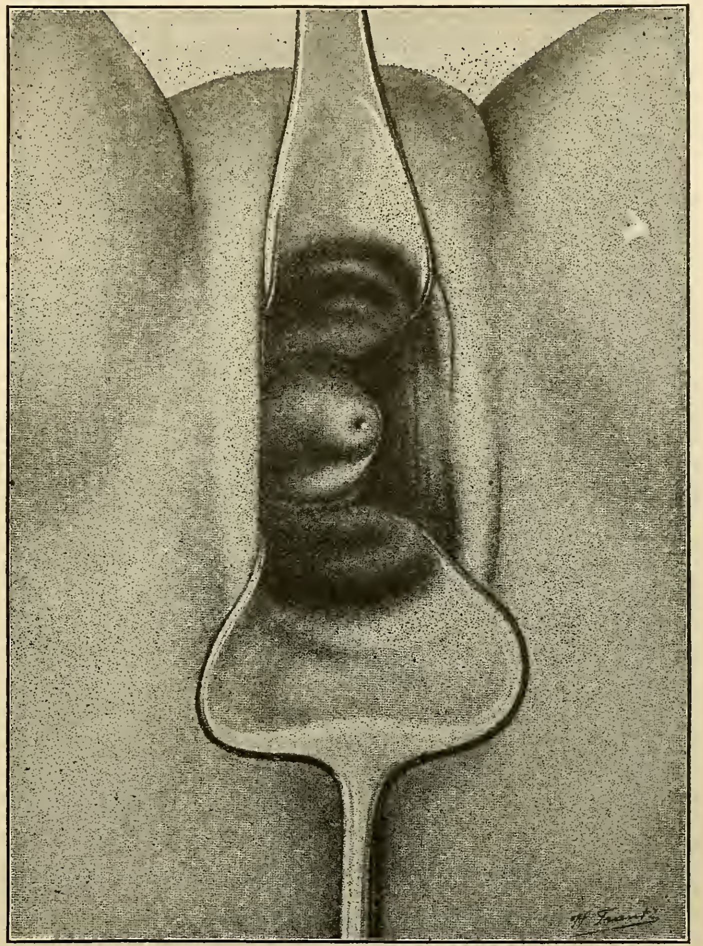


Fig. 1.—Conical cervix. Punctiform orifice. (*S. Pozzi.*)
(Surgery, Gynecology and Obstetrics.)

weak, undeveloped musculature and blood-vessel system, the normal physiological process of development after puberty has failed, is arrested or slow, it is reasonable to conclude that it is possible this uterus can be stimulated to further development by artificial means.

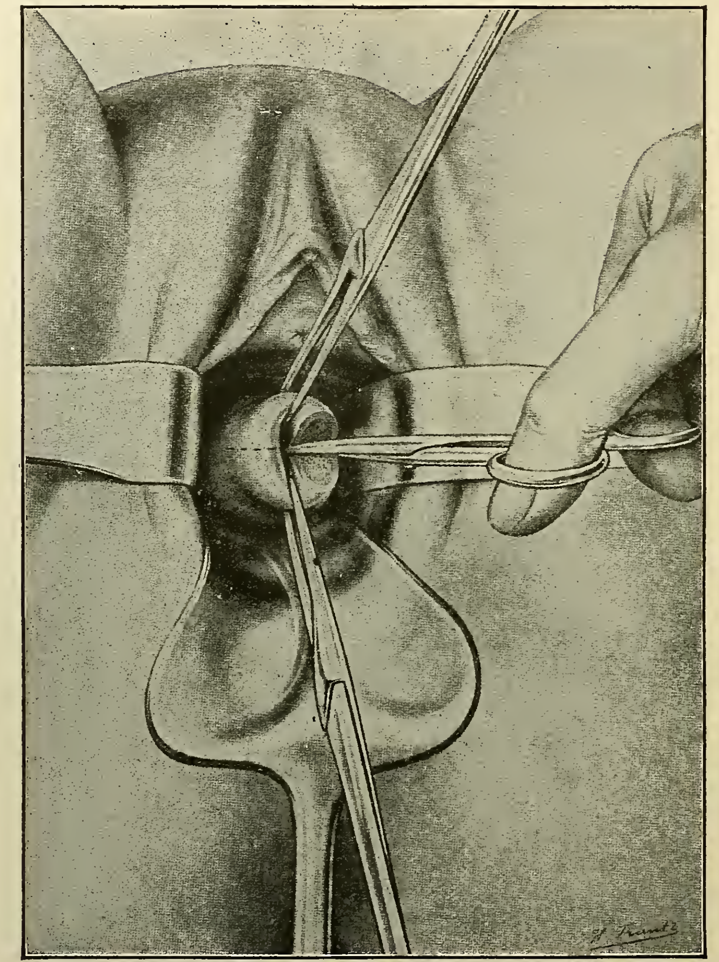


Fig. 2.—Bilateral incision of the cervix. (*S. Pozzi.*) (Surgery, Gynecology and Obstetrics.)

Every gynecologist has noted that in certain instances women who have suffered with dysmenorrhea have been relieved after **marriage,** because of coitus and development of the sexual passion, the change in **sexual life** being the added stimulus to uterine development. Also, if the woman is fortunate enough to become pregnant and either goes to term or aborts, relief follows. Beyea (Univ. of Penna. Med. Bull., May, 1910).

The field of **surgical treatment** for dysmenorrhea is a large one and frequently will result in the happiest consequences. The chief objects of surgical treatment are to relieve obstruction, to produce stimulation, and to improve local nutrition.

The causes of obstruction have been mentioned, and should be removed as completely as possible; an imperforate hymen should be divided or dissected away; obstructing bands in the vagina should be cut and a series of vaginal dilators worn until the normal caliber of the vagina has been restored. Bands and constrictions at the os externum or internum should be divided, a narrow cervical canal should be dilated and curetted, especially when the glands are the seat of exuberant or unhealthy secretion.

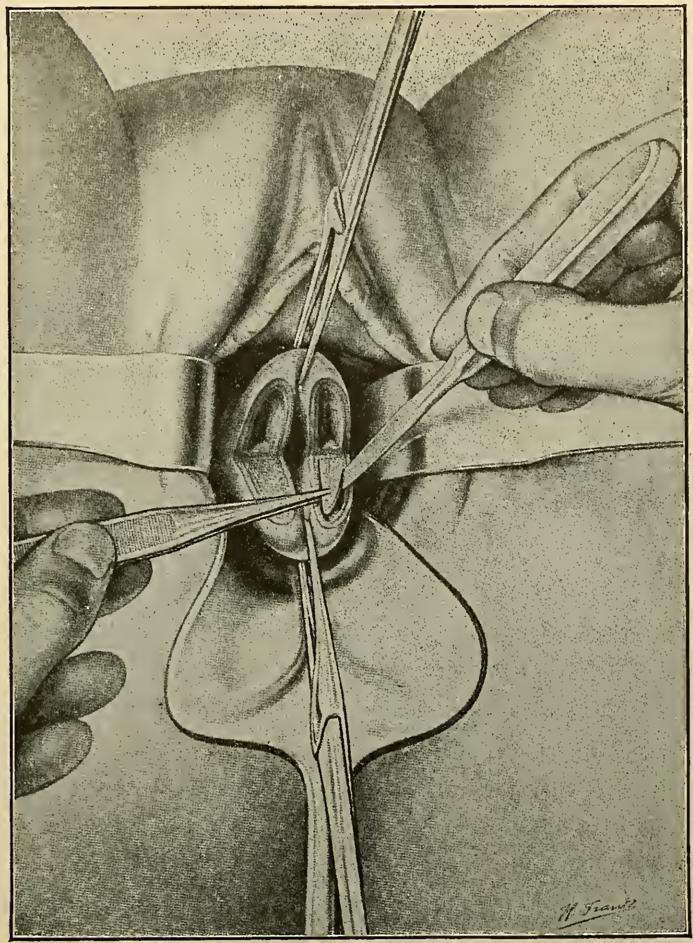


Fig. 3.—Hollowing out of the cut surfaces of the cervix. (*S. Pozzi.*)
(Surgery, Gynecology and Obstetrics.)

There is an infantile type of the internal genitalia which consists essentially in the conical shape of the cervix with extremely small lumen and exaggerated anteflexion of the uterus, all of which may be encountered in women otherwise well developed and without atrophy of the uterus, although it is more common with other signs of infantilism. Dysmenorrhea is the rule and also sterility. The kinking of the cervix causes stagnation of mucus with consequent inflammation, obstructing the lumen still more. In the writer's operation he incises the cervix on each side and excises a small triangular piece from the center of each of the four raw surfaces made by the two incisions. He then sutures the mucosa of the lumen to the mucosa on the outer aspect of the cervix, thus suturing the four raw surfaces and leaving the lumen of the cervix widely gaping. In his experience with 54 cases in which he has applied this technique, 14 of the patients have conceived since, and he never has noticed any interference with delivery from the rigidity of the cervix. S. Pozzi (Bull. de l'Acad. de Méd., Nov. 9, 1909).

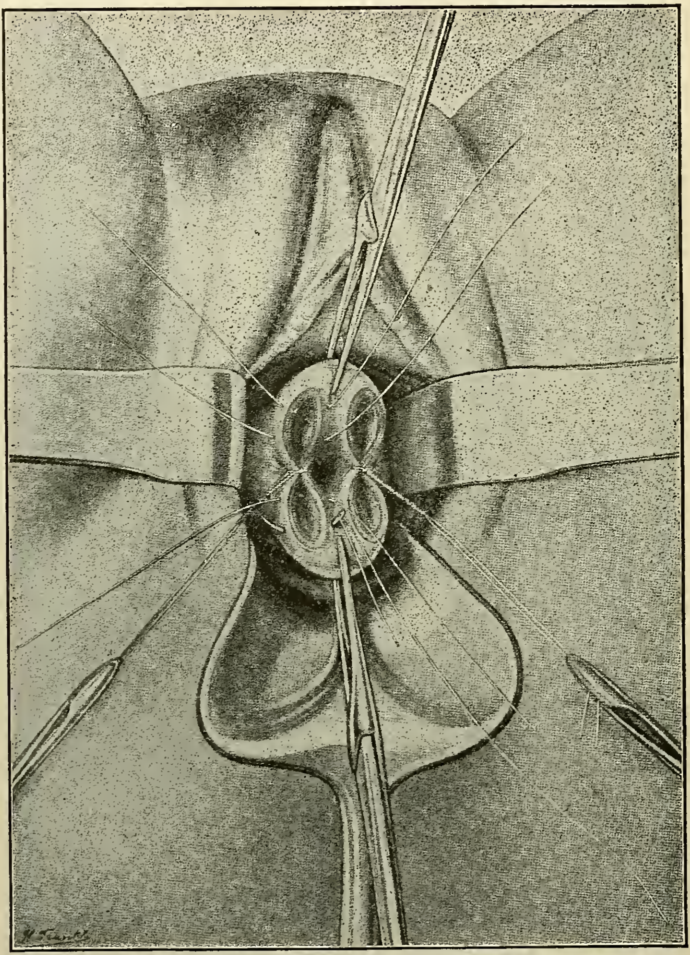


Fig. 4.—Introduction of the stitches. The commissural stitches are drawn tight. (*S. Pozzi.*) (Surgery, Gynecology and Obstetrics.)

In many cases of dysmenorrhea in unmarried women, examination of the womb and adnexa is absolutely negative. There being an intimate connection between the breasts and ovaries, the writer has tried the almost forgotten instructions of Polano. A **suction cup** 7 to 8 cm. in diameter is applied daily for half an hour, beginning four to five days before the appearance of the menses. The patients soon learn to use this instrument and the slight pain experienced at first is soon disregarded. The results are excellent and in by far the majority of cases the colicky pains either do not appear or are much ameliorated. Even in severe cases the relief experienced is remarkable. Flatau (Klin. therap. Woch., March 28, 1910).

In 73 cases of dysmenorrhea and sterility the writer resorted to the operation described by Dudley, preceded by wide dilatation of the cervix and **light curettage.** The denudation of the anterior lip was omitted, but the splitting of the posterior lip, excision of two wedge-shaped pieces, and suture were performed typically. In all cases the husband's semen was first examined. In 21 private cases 84 per cent. were relieved of their dysmenorrhea and 42 per cent. of their sterility. Of 52 ward patients 55 per cent. were relieved of dysmenorrhea and 17 per cent. of sterility. The writer holds that the operation is satisfactory in both sterility and dysmenorrhea, but that it is of greater service in the relief of the second type. The scar offers no hindrance to subsequent parturition. S. M. Brickner (Surg., Gynec. and Obstet., Nov., 1911).

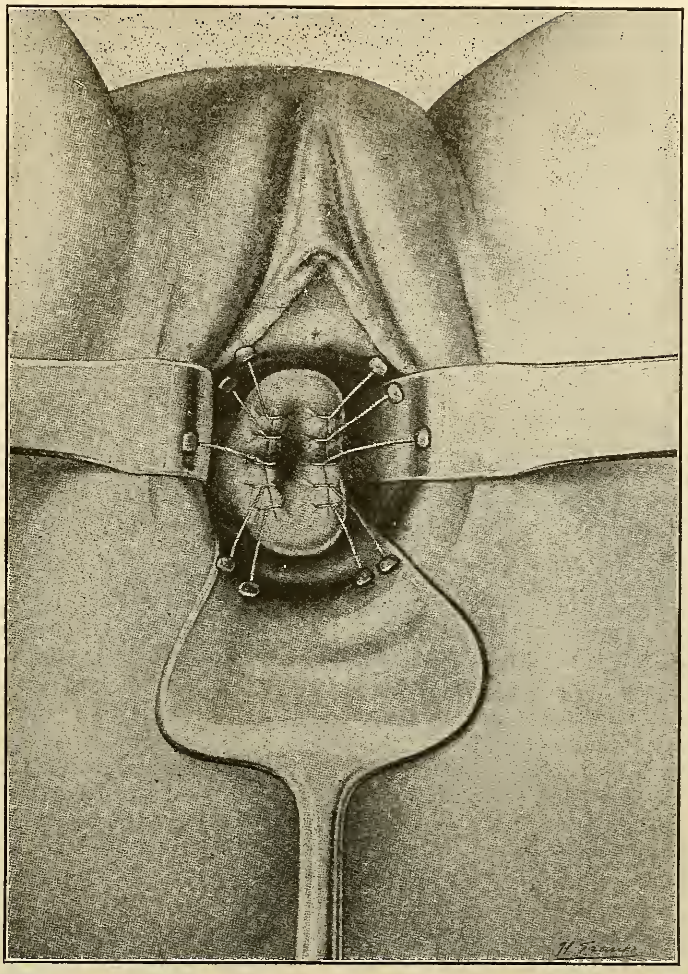


Fig. 5.—The operation finished. All the stitches have been drawn tight and the leaden guards applied. (*S. Pozzi.*)
(Surgery, Gynecology and Obstetrics.)

Obstruction from the presence of tumors within the uterus which may cause excessive pain can be relieved only by their removal, and the requisite operations must also be performed if the dysmenorrhea is caused by displacements of the uterus or its incarceration by inflammatory exudate. Any less radical form of treatment for such conditions has, in the experience of the writer, proved to be only time-consuming and futile.

Dysmenorrhea may be primary or secondary. In primary dysmenorrhea, the pelvic organs are either normal or else merely poorly developed. In secondary dysmenorrhea, marked pathological changes are present in the pelvic organs, and these pathological changes are the cause of dysmenorrhea. The most frequent pathological conditions causing dysmenorrhea are: (1) pelvic inflammatory disease; (2) retrodisplacement of the uterus; (3) myomata, especially the submucous variety.

Primary dysmenorrhea often dates from debilitating illnesses, and is often apparently caused by anemia, malnutrition, and neurasthenia.

In 40 per cent. of all cases of dysmenorrhea in which the pelvic organs are normal, or else merely poorly developed, successful results may be expected from dilatation of the cervix and curettement of the endometrium. By "successful results" is meant entire or very great relief from dysmenorrhea for a year or more, with or without subsequent return of the trouble. No relief whatsoever may be expected in 30 per cent. of the cases. The relief in the remaining 30 per cent. varies in degree and duration.

The presence of anemia, malnutrition, or neurasthenia does not necessarily cause a bad prognosis after dilatation and curettement; but in order to obtain a successful result from the operation, these conditions must be rectified. If the patient's general condition is not improved, little relief will be given by the operation. The prognosis is better in those cases in which the pains (1) begin the day of flow or the day before, (2) are sharp in character, and (3) last but a day or two. The prognosis is worse when the pains (1) begin several days before the flow appears, (2) are dull in character, and (3) last for several days or throughout the flow.

Every operation should be preceded by a careful examination under ether. If the organs are not normal, the prognosis is worse. When the history points to inflammatory trouble, even though none can be recognized at the ether examination, its possible existence should be carefully considered. If in such cases an exploratory laparotomy is not thought advisable, it is best to limit operative procedures to dilatation of the cervix and omit curettement.

In dysmenorrhea recurring after a period of relief following dilatation and curettement, the possibility of the new appearance of a pathological condition in the pelvis, *e.g.*, a retrodisplacement, should be carefully considered.

When the pelvic organs are poorly developed, the prognosis for relief after dilatation and curettement is much worse than when the organs are normally developed. Apparently maldevelopment of the pelvic organs causes dysmenorrhea. Chronic endometritis is rarely present in cases of dysmenorrhea, unless there is at the same time an inflammatory condition of tubes or ovaries. Chronic endometritis alone is rarely a cause of dysmenorrhea.

Sterility is relieved by dilatation and curettement in but 15 per cent. of the cases of sterile married women who are in the child-bearing period. The relief of dysmenorrhea does not necessarily mean the relief of the sterility, and, *vice versâ,* sterility may apparently be relieved without relief of the dysmenorrhea. The relationship between dysmenorrhea and sterility seems an accidental one, and of no significance.

While dilatation and curettement in the majority of cases are perfectly safe, when the technique of the operator is imperfect, either on account of unfavorable surroundings or lack of proper skill, it may be exceedingly dangerous. G. R. Holden (Amer. Medicine, Nov. 4, 1905).

The pain of dysmenorrhea is sometimes relieved within a few minutes after the application of a 20 per cent. cocaine solution to certain areas in the nasal mucous membrane which are composed of erectile tissue, and which always become swollen, hyperemic and hyperesthetic, during each menstrual period. Where the pain is due to some uterine displacement, inflammation, or other local condition, application of cocaine to these nasal areas has no effect. In cases followed by relief a permanent cure may often be affected by cauterization or other suitable rhinological treatment. Brettauer (Amer. Jour. of Obstet., vol. lxiv, p. 215, 1911).

The use of pessaries for the relief of displacements, while it frequently modifies the dysmenorrhea, seldom cures the displacements; hence, such means are used with far less frequency than formerly. The same may be said of the cutting operations which were once so popular for the relief of dysmenorrhea supposed to be the results of anteflexion of the uterus.

Stimulation of the uterus and improvement of its nutrition are often effectively produced by the passage of **graduated sounds** into its canal, the use of the **steel dilators, curettage,** and occasionally by the abstraction of blood from the cervix with **leeches,** or by **punctures** or **scarification,** especially when the cervix is congested and the menstrual flow is scanty.

Andrew F. Currier,
New York.

DYSPEPSIA. See Stomach, Diseases of.

E

EAR, DISEASES OF. See External Ear, Internal Ear, and Middle Ear.

ECHINOCOCCUS CYST. See Parasites, Diseases Due to.

ECLAMPSIA. See Puerperal Eclampsia.

ECZEMA.—DEFINITION.— Eczema may be either an acute, subacute, or chronic inflammatory disease of the skin, usually characterized in its earliest stages by the appearances of erythema, papules, vesicles, or pustules or a combination of two or more of these lesions. It is attended with a variable degree of thickening and infiltration of the cutaneous tissues, terminating either in discharge with the formation of crusts or in absorption or in desquamation.

VARIETIES.—The elementary, or primary, varieties are the erythematous, papular, vesicular, and pustular, or the first outbreak may show a mixture of these several types. In many cases the beginning lesions or type soon lose their characters and the disease develops into the common clinical varieties: eczema rubrum or eczema squamosum. Other clinical or secondary types met with are eczema fissum, eczema sclerosum, and eczema verrucosum.

SYMPTOMS. — The *erythematous* type of eczema—also called eczema erythematosum—is most frequently seen upon the face, although it may make its appearance upon any other region or may be more or less general. It begins as a single hyperemic area, or several areas may appear simultaneously, usually upon one region. The areas may be small or large, irregularly outlined, ill defined, and attended with slight or considerable swelling and even edema. There is more or less itching and burning. The eruption soon becomes pronounced, the parts reddened, somewhat thickened, and here and there a little scaly. There may also be, here and there (as a result of rubbing and scratching, or spontaneously), a tendency to serous oozing. The affected skin is harsh, dry, and reddish or violaceous in color. It often persists in this form, and the skin may become considerably thickened and infiltrated. The swelling and edema which are often first present may subside, to a great extent at least, or these symptoms may reappear from time to time whenever there is an acute exacerbation. The parts may become quite scaly, and constitute a mild or well-marked scaly eczema: eczema squamosum. Occasionally, as a result of constant irritation, rubbing, and scratching, or from other causes, the parts become moist, markedly inflamed, with more or less crusting, constituting eczema rubrum.

The *papular* type of the disease, or eczema papulosum, presents itself as one or more aggregations of closely set papules, pinpoint to pinhead, or slightly larger, in size. The disease may also show itself as more or less discrete papules, with here and there aggregations. In color the lesions are bright or deep red or violaceous, with often a few vesicles or pustules interspersed. Itching is usually intense.

The extremities and the hands, especially about the joints, are its favorite sites. The course of this type is essentially chronic, some lesions disappearing and others appearing, and thus persisting for several months or indefinitely. In some instances, especially in some areas, the papules become so thickly crowded that a solid patch results, becoming more or less scaly—eczema squamosum. Or, at times such a patch may develop into eczema rubrum.

The *vesicular* type of the disease, or eczema vesiculosum, may show itself on one or more regions, and consists of aggregated or closely crowded pinpoint- to pea- sized vesicles, with here and there discrete lesions, and at times with papules and pustules interspersed. It is usually a markedly inflammatory type, with considerable edema and swelling. Solid sheets of eruption may form. The vesicles usually rupture in the course of a few hours or days, new outbreaks occurring, or a raw, weeping, more or less crusted surface resulting. The oozing may be continuous or the process may decline, to remain quiescent or to break forth rapidly with repeated vesicular crops. Considerable thickening may take place and with the oozing and crusting make up a picture of the common clinical type: eczema rubrum. The face and scalp of infants, the neck, flexor surfaces, and fingers are the more common sites for the vesicular type. Its course is usually chronic, with several acute exacerbations, or, as already described, it may pass sooner or later into the common clinical type: eczema rubrum.

The *pustular* variety of eczema, or eczema pustulosum or impetiginosum, is less frequently met with than the other varieties of the disease. Its common site is the scalp, especially in infants. It may develop from the vesicular variety, or, as more commonly the case, begin as closely set pinpoint to pinhead or larger sized pustules, or a mixture of vesicles and pustules may be noticed. In symptomatology it is similar to eczema vesiculosum, except that the lesions, instead of containing serum, contain pus. As in the vesicular type, the same disposition to the rupture of the pustules is observed, and there is often a tendency to develop into the type known as eczema rubrum. More or less crusting is usually a conspicuous feature. The ill-nourished and strumous persons are its most common subjects. The type is essentially chronic.

The *squamous* type of eczema, or eczema squamosum, is a clinical variety frequently met with, characterized by redness, infiltration, and more or less scaliness, with, especially when about the joints, more or less fissuring. The itching is variable, sometimes intense, and at other times slight. This variety is usually a development from the erythematous or papular types, and, like other types of the disease, is persistent and chronic.

Eczema rubrum, the oozing type of eczema, or somewhat dry, raw-looking type of eczema, usually results from a pre-existing vesicular or pustular eczema. It is characterized by a red, weeping, oozing, raw-looking surface, with more or less infiltration of the cutaneous tissues. In some cases there is a combination of weeping raw surface with crusted areas. In other cases the weeping nature of the disease is a conspicuous feature, crusting scarcely having time to form: eczema madidans. Its most frequent sites are the face and scalp of children and the legs of adults; in the latter in those especially advancing in years. In these cases of eczema of the lower legs varicose veins are often present as a precursory and concomitant condition. It is essentially chronic, showing little, if any, disposition to disappear spontaneously, although it may be somewhat variable. The degree of inflammation varies from time to time.

The *fissured* type of eczema, or eczema fissum or eczema rimosum, is that type of eczema in which cracking or fissuring of the skin is the most conspicuous feature. It is common about the joints, especially about the fingers, and in most cases is a part of an apparently slight erythematous eczema. Fissuring may occur in any type of the disease, especially when about the joints; but in most cases it is but slight in character. It is a persistent type of the disease, usually disappearing in part or more or less completely in warm weather. A somewhat analogous or allied variety of eczema is the so-called crackled eczema. This is usually a mild, subacute, erythematous eczema, involving large regions or the entire surface, numerous superficial cracks through the upper epiderm showing over the fissured surface.

Eczema *sclerosum* and eczema *verrucosum* are somewhat rare varieties of the disease. These types are usually seen about the ankles, lower leg, or feet. They commonly result from a pre-existing papular eczema. In many respects these types are analogous in their symptomatology: there is considerable thickening and board-like hardness, with, as a rule, much infiltration, but with the inflammatory element slight or comparatively so. The surface is rough, hard, and somewhat horny to the feel, and in the verrucous variety there is added to these several symptoms a variable degree of papillary hypertrophy, the surface having a distinctly warty appearance. Both types are essentially chronic and rebellious to treatment, demanding the strongest application.

Infantile Eczema.—The disease is common in infants and young children. It is unusual, comparatively speaking, in children past the age of 6. Even in those cases in which the disease begins in the first or second year and is persistent, it tends to decline spontaneously toward the age of 5 or 6, or even earlier, or, at least, at this period it will usually respond rapidly to any mild or indifferent application. The disease presents no special characteristics in the young, except that in the majority of such cases the inflammatory element is apt to be more marked. In by far the larger proportion of cases the face or the face and scalp is the seat of the disease; eczema of the region of the genitalia and anal cleft is also not infrequent.

All cases of infantile eczema will usually do well under treatment, although a disposition in many cases is shown toward relapse till the age of 4 to 6 is reached.

In eczema in infants and young children occurring about the legs and arms, usually as a vesicopapular or papular eruption, discrete and patchy, the disease is often obstinate,—much more so, as a rule, than in those cases where the disease is limited to the face or face and scalp. The vesicular, vesicopapular, and moist or crusted inflammatory types—eczema rubrum—seem most frequent in the young.

Regional Eczema.—It is usual to describe eczema as it appears upon different regions, as, for instance, the hands, face, scrotum, legs, etc.; but the disease in reality differs little, certainly not materially, as it occurs upon different parts. The description of the several types of the disease as already given suffices.

It is noted that the most common seats for eczema in those of the active age, between 21 and 50, is about the hands; less frequently about the face or the scalp; the scrotum is not an uncommon site, and also the anal region.

In those past the age of 50 the most common site is the lower leg, although eczema of the face is not infrequently met with.

GENERAL SYMPTOMATOLOGY.—The subjective symptoms in eczema are itching, burning, and a sensation of heat. These may be severally present, or, as is more commonly the case, one is predominant. The degree varies, sometimes slight and at other times almost unbearable. As a rule, there are no constitutional symptoms so called in eczema cases. In extensive general acute eczema there may be slight febrile action and sometimes slight chilliness at the outbreak of the attack. The degree of inflammatory actions varies in the same case from time to time and in different cases. The disease may be acute both in type and in course, running to an end in several weeks or one or two months. As a rule, however, whatever the type of the inflammatory process—acute, subacute, or chronic—the disease is persistent and long continued, with, in most cases, little, if any, tendency to disappear spontaneously. Seasons often have an influence, the disease usually being less active or partly or completely disappearing in the summer weather. On the other hand, there are cases of the disease met with that are at their worst in summer time, and frequently disappear in the colder weather; such instances are, however, exceptional.

ETIOLOGY.—The consensus of opinion points to both external and constitutional causes as active factors in most cases of the disease. The possibility and even probability of this disease's being due to a parasite is quite generally believed at the present time.

Gilchrist and Sabouraud have noted the frequency with which streptococci occur in skin lesions. In more than 100 cases it was possible to detect staphylococci in 53.7 per cent.; 27 of these cases were eczema, and in these streptococci were present 17 times. In order to determine in what proportion of normal skins streptococci were present, 160 areas in 55 human beings were studied, and streptococci were found in 7.5 per cent. They are most frequent in the axilla and on the back. These streptococci resemble exactly those found in skin lesions. The artificial forms of dermatitis are sometimes sterile, and sometimes bacteria in considerable numbers can be obtained from them. Frederic (Münch. med. Woch., Nu. 38, 1901).

For a time the idea of a pathogenic microbe of eczematous eruptions, so strongly advocated by Unna, seemed to account for them, but unfortunately this theory has not been confirmed by precise observations, and must be abandoned, at least provisionally. But if we apply ourselves to the clinical analysis of facts, we perceive that true eczematous eruptions arise now in consequence of external irritations, again from various intoxications, autointoxications, organic diseases, nervous shocks, etc. The most divergent causes appear to possess the power of evoking them. We are disposed for the moment to view true vesicular eczema as a pure cutaneous reaction. Brocq (Ann. de dermat. et de syphil., March, 1903).

In infantile eczema and in opposition to Hebra's local irritation theory, many have emphasized the parasitic theory, holding that the cocci penetrate into the lymph-spaces and there produce their toxins. Slight traumatisms would favor this, and the susceptibility of the infant's skin is thereby increased, causing persistent and recurrent attacks. As to whether the food plays a part in the production of eczema, if coarse pathological changes exist in the digestive apparatus the food may act as a toxin-producing factor in breast-fed infants, as well as in those fed otherwise. C. A. Simpson (Jour. Amer. Med. Assoc., April 6, 1912).

Among the constitutional influences which are or seem to be of some importance as predisposing or active factors are gout, rheumatism, disorders of digestion or assimilation, dentition, struma, general debility, and loss of nervous tone.

The most rational view, based on clinical observation, is to consider eczema an external manifestation of some internal disorder. Constitutional conditions are the underlying cause and the presence of bacteria in the external lesions may result from secondary infection and not act as cause. The French authors lay considerable stress on hereditary influences and that parental arthritis, gout, obesity, asthma, and various neuropathic conditions tend to favor eczema in the offspring. That this view is based on facts is corroborated by every observer's clinical experience. Gaucher finds an inhibition of metabolism in every case and regards eczema as an autointoxication, the poisons being eliminated through the skin. I. A. Abt (Jour. Amer. Med. Assoc., Sept. 11, 1909).

Immoderate habits in the use of certain foods, drinks, and drugs also indirectly or directly have an influence, such as alcoholic drinks, narcotic drugs, and excessive tea- or coffee- drinking.

Overwork, especially of a mental character, in those of hereditary eczematous tendency will often be provocative of an attack. That the hereditary disposition to the disease exists in many families cannot be denied.

Among the external exciting factors may be mentioned cold and heat, especially the former; sharp, biting winds, and too liberal use of certain soaps; the handling of dyestuffs, chemical irritants, and the like; vaccination, and exposure to certain plants. Having the hands frequently in water, as with washerwomen, the handling of sugar and flour, and repeated antiseptic cleansing of the hands often bring about the various conditions of eczema of these parts known respectively under the names of washerwomen's itch, bakers' itch, and grocers' itch, and surgeons' eczema.

Eczema may occur in anyone if the local causal irritation is prolonged or sufficiently often repeated, as is shown in many cases of occupation eczema, in which the inflammation appears only after a shorter or longer period of immunity. Moreover, in local eczema it is often difficult to detect the exciting cause; unless we can entirely exclude such, the assumption of an internal cause is not justified. While he is not prepared to accept the theory of a parasitic origin of the disease, the writer is willing to admit an important rôle to micro-organisms, which he believes may often transform a simple local inflammation into a chronic eczema. The fact that antiseptic substances, like tar, resorcin, etc., are often of great service, supports this view. He does not deny that eczema may arise from causes within the body, but he thinks that by far the greater proportion of cases arise from external irritation. M. B. Hartzell (Jour. Amer. Med. Assoc., Nov. 28, 1908).

There are 74 varieties of eczema associated with a corresponding number of callings. There is a "cement itch," a "baker's itch," a "washerwoman's itch." Wool and cotton spinners have theirs, set up by irritating oils, which also cause eruptions in other occupations. The great majority of the lesions are naturally due to irritating chemicals of the most varied description in connection with the industrial arts. No less than 12 varieties of exotic wood are able to cause lesions in cabinet makers, turners, and other wood workers. Herxheimer (Deut. med. Woch., Jan. 4, 1912).

Fully one-quarter of all cases of eczema are of definite external origin. Almost one-sixth of all cases of this affection are caused by the occupation of the individual. Micro-organisms are apparently not the cause of eczema, but probably play a secondary rôle in the affection. The largest number of cases of the so-called occupation eczemas are seen in the workers in the household and next most frequently in laborers. Practically every occupation and every irritant may produce an eczema. The portions of the skin exposed to the irritant determines the site of the outbreak. Knowles (Jour. of Cutan. Dis., Jan., 1913).

So far as is known the disease does not possess contagious properties, and in a disease so frequent as this if such existed it would have been clearly demonstrated; the acceptance of a parasitic cause, however, carries with it the possibility of communicability under favoring conditions.

In a room containing 35 girls between 11 and 14 years of age, 29 presented seborrheic eczema, the foci being in the face. The course was tedious owing to the tendency to recurrence. The other schoolrooms contained only a few isolated cases. Bruhns and Cohn (Berl. klin. Woch., Sept. 30, 1912).

In some cases of markedly inflammatory eczema, especially when of the pustular type, swelling of the neighboring lymphatic glands is noticed, but this rarely leads to suppurative change, the swelling and pain disappearing as soon as the inflammatory symptoms have abated. In some cases of eczema a condition of furunculosis is occasionally observed.

> Case of chronic eczema of the crurogenital region followed by fatal gangrene. Small superficial ulcers the size of a lentil developed over the sacrum and the temperature began to rise in the evenings to 101° or 102° F. (38.3° or 38.9° C.). Three days later the abdomen and thighs presented a remarkable appearance. The whole of the raw surface, which was now of a deep-red color, was picked out by clean-cut circular ulcerations the size of a lentil, which looked as though they had been deeply punched out of the skin. Each little ulcer was filled with yellowish pus, and the whole surface was studded with these necrotic foci. In a day or two adjoining ulcers began to coalesce, forming little troughs in the skin, while later on their bases dried up into blackish scabs, some of which toward the end were thrown off and replaced by granulation tissue. The general condition of the patient became very grave when the ulceration appeared, a typical septicemic temperature developed, and the pulse ran more and more rapidly and became feebler by degrees. A day or two before death the border of the diseased skin became sharply defined, with a black, ribbon-like scab of dry gangrene.
>
> The *Bacillus pyocyaneus* was found microscopically in enormous numbers in the exudation, and was recovered by cultures from the exudation, spleen, liver, and blood of the heart. C. H. Lancashire (Brit. Jour. of Dermat., July, 1910).
>
> Case of hemorrhagic nephritis following impetiginous eczema in a girl, 10 years of age. Recovery took place in a short time. Halburstadt (Monats. f. Kinderheilk., Bd. x, Nu. 10, 1912).

PATHOLOGICAL ANATOMY.—Eczema is essentially a catarrhal inflammation of the skin, and is seated chiefly in the rete and papillary layer; in long-continued and severe cases the lower part of the corium and even the subcutaneous tissue may be more or less involved, but never destructively. Hyperemia and exudation are to be found in all cases, either as punctate, localized, or more or less diffused. The vascular changes are the same as observed in all inflammations.

DIAGNOSIS.—Eczema is to be distinguished chiefly from erysipelas, psoriasis, seborrhea, sycosis, scabies, and ringworm.

Erysipelas. — Markedly acute eczema about the face sometimes presents early in the course of the attack a resemblance to erysipelas, but in the latter disease the border is sharply defined and elevated; it usually starts from one point and spreads rapidly, and is accompanied by systemic symptoms of more or less violence.

Psoriasis as commonly met with is not difficult to differentiate. The numerous, variously sized, sharply defined scaly patches, of general distribution, of psoriasis make this disease sufficiently characteristic. The face and hands are rarely involved, or only to a slight extent, at least, in psoriasis, while these regions are favorite sites for eczema. The psoriasic eruption often is seen most markedly on the extensors of the arms and legs, especially about the elbows and knees; eczema is more common in the flexures. Psoriasis is usually markedly scaly, eczema rarely so. In occasional instances psoriasis is limited to the scalp, appearing here as several or numerous, variously sized, scaly areas, resembling squamous eczema of this part. The same differential characters can be here recognized, if the case is studied, as when seated upon other parts. Moreover, a careful examination will usually disclose the presence of several small or moderately sized characteristic psoriasic patches on the limbs, especially about the elbows and knees. Eczema of the scaly type is usually seated upon one region, is rarely generalized in its distribution, and the area or areas are rarely sharply defined. Itching is the rule in eczema and is often absent or slight in psoriasis. In many cases of chronic scaly eczema there is often a history of gummy oozing, which does not obtain in psoriasis. The eruption produced in the parasitic diseases, scabies and pediculosis, is essentially eczematous in many of its characters, but is usually multiform, consisting of papules and pustules, the latter often being large in size. The distribution of the eruption in these parasitic diseases will often be sufficiently characteristic, and suspicion may be confirmed by the finding of the pediculus in pediculosis or by the burrow in scabies. Seborrhea at times bears close resemblance to a mild eczema, more especially as it occurs on the scalp. The seborrheic disease is, however, rarely inflammatory, except accidentally so; the scales are greasy, and there is lack of infiltration and thickening.

Sycosis.—Eczema of the bearded face may be mistaken for sycosis, but this latter disease is essentially one of the hair-follicles—folliculitis barbæ—limited to the hairy region of the face, and is rarely itchy. Eczema, on the other hand, is seldom limited to this region, but extends on to the non-hairy parts of the face, is not follicular, and is very itchy. Ringworm can scarcely be confounded with eczema, as eczema is seldom sharply defined, rarely ring-shaped, but is diffused, with no tendency to clear up in the center. In cases of a doubtful character microscopic examination of the scales will be sure to differentiate.

Dermatitis.—Dermatitis is sometimes with difficulty distinguished from eczema, as the symptoms of mild dermatitis are essentially the same as those of eczema; in fact, these cases may be looked upon as artificial eczemas. Eczema rarely, if ever, shows large vesicle or bleb formation as found in the severe types of dermatitis, more particularly from rhus. The history of the case will often throw light upon the diagnosis. In those eczematously inclined, however, what may be a true artificial dermatitis in the beginning may terminate in a veritable stubborn eczema.

Among other diseases that should not be confounded may be mentioned rosacea, erythema, urticaria, herpes zoster, lichen planus, lichen ruber, and impetigo contagiosa.

PROGNOSIS.—Eczema, while often most intractable, cannot be said to be incurable. It may recur like any other disease to which a person may be prone. Under favorable circumstances mild cases yield quite readily. During the course of treatment the disease may show slight relapses, but each succeeding one is usually noted to be of a milder and less obstinate character. It is difficult, in the individual case, to state an opinion, especially as to the duration of treatment. Several factors should influence the prognosis: the extent involved, the duration, previous variability, the nature of the exciting and predisposing causes, and whether these can be readily managed, and, finally, and of great importance, the care and attention the patient gives to the carrying out of the treatment advised.

The mystery of the sudden deaths of children with eczema of the scalp and face is discussed by the writer. In one such case the autopsy revealed an unsuspected streptococcic focus in one lung, the action, at a distance, of these germs having induced slight endocarditis and pleural effusion. In another case an infant with eczema exhibited attacks of heart weakness, possibly from a similar action of the germs on the heart muscle. Another child of eleven months was in his care for recurring eczema of the scalp and face. The child was brought to him, after two months' absence, on account of a new patch on the cheek, and he was impressed with the dull look in the eyes, but nothing abnormal could be detected in lungs or heart. The cervical glands were swollen. A salve of ichthyol and zinc oxide was ordered. The child seemed unusually quiet, and was found dead the second morning. Staphylococci were discovered in the cutaneous lesions and in the internal organs. Their numbers were not large, but it is possible that the eczema may have generated toxins, similarly to extensive burns, which may have induced an actual toxic form of staphylococcus myosis. This assumption was confirmed by a number of experiments on animals. Infection with the staphylococcus alone did not cause, by any means, such severe symptoms as when the staphylococcus infection was supplemented by a cutaneous lesion, such as a croton-oil blister. The heart seemed to suffer particularly in these cases. The researches reported emphasize the importance of careful oversight of the heart action in cases of extensive eczema. Possibly the blood-pressure might afford useful information. J. Bernheim-Karrer (Jahrb. für Kinderheilk., Bd. lxii, Nu. 6, 1905).

The writers have traced the fate of 100 children between 3 and 11 years of age, known to have suffered from chronic eczema during infancy. The majority were found in apparent health. No special tendency to the rheumatic or gouty diathesis could be detected either in patients or their parents and no evidence of special overfeeding. Another point brought out is the frequency of spasmophilic phenomena in infants with the exudative diathesis. The coincidence is too striking to be merely casual; it seemed rather as if both were clinical manifestations of one and the same diathesis. Moro and Koll (Monats. f. Kinderheilk., Bd. ix, Nu. 8, 1901).

TREATMENT.—There has been great diversity of views as to the methods of treatment,—*e.g.,* as to whether it should be external or constitutional. The conservative course, and that which seems to give the best results, is that which places reliance upon conjoint local and systemic measures. It is not improbable that there are some cases met with which persist without any constitutional cause, or the latter has already disappeared, and in such instances external treatment alone will bring about permanent relief. There are certain general or hygienic measures which should receive attention. The **diet** should be plain, but nutritious, all fancy dishes and indigestible meats and foods being avoided as much as possible.

The writer has tried Finkelstein's method and reports excellent results. Its purpose is to exclude salt from the food; the experiences related confirm the efficacy of this measure, even for older children. The writer's patients were between 2 and 6 years old. In one case local measures and **deprivation of salt** arrested the eczema, which healed completely in three weeks, while a previous attack had resisted all measures for several months. In all such cases the eczema was of the "exudative diathesis" type. Geissler (Münch. med. Woch., Feb. 23, 1909).

The writer found **diet** of rice, bread, butter, and water effective in acute generalized eczema. Bulkley (Med. Record, Jan. 28, 1911).

The general practitioner should look upon eczema as a curable disease, but only when properly treated. It is wrong to starve the patients, forbidding articles of food without scientific ground. The patient should be well fed to increase albumin in the serum to form antibodies to oppose the toxic elements. Only indigestible and badly preserved articles of food are to be avoided. The general practitioner should renounce the false idea, or rather the superstition that washing and cleansing eczematous surfaces are injurious. The affected parts should be cleaned and kept aseptic like other suppurating wounds. Solutions of **bicarbonate** or of **biborate of sodium,** or even a mild soap accomplish the purpose.

For an acute eczema bathing with a 2 per cent. solution of **subacetate of aluminum** proved beneficial. After bathing, the surface was covered with **starch** *or* **talcum powder.** For a papular and vesicular eczema applications of **liniment of ichthyol** or of **carbonate of zinc** were useful. In recurrent vesicular eczema, painting the surface with **tincture of iodine** to sterilize the surface had given very good results. Rhagades must be touched with **silver nitrate,** from 3 to 5 per cent. solution. Many different preparations in the form of salves, pastes, gelatins, lotions, are recommended in textbooks, but the physician must familiarize himself with their use. A. Ravogli (N. Y. Med. Jour., March 15, 1913).

Pork and salted meats, veal, pastries, strong acids or acid fruits, gravies, cheese, sauces, condiments, etc., and the excessive drinking of tea or coffee are to be eschewed. Beer, wine, and spirits are also to be avoided.

Outdoor life is to be commended in suitable weather, and **exercise,** especially systematic in character, is of great value.

As to constitutional remedies, it may be said that there are no specifics, although **arsenic** seems at times of special value in chronic, sluggish, papular, and erythematosquamous types. Each case must be carefully studied, and the predisposing factor or factors, if possible, discovered, and the treatment suitable instituted. When the itching is so intense as to prevent sleep, recourse may be had to the **bromides, phenacetin, chloral, sulphonal, trional,** and the like; opiates are apt to cause aggravation.

Among the tonics that are often of value may be mentioned **codliver oil, hypophosphites, quinine, nux vomica,** the **vegetable bitters, iron, arsenic,** and **manganese.** Arsenic should never be given in the acute type, or in any case in which the disease is of the spreading or active character. Among alkalies, especially useful in gouty and rheumatic cases, may be mentioned **sodium salicylate, potassium bicarbonate, sodium bicarbonate,** and the **lithium salts.**

Among alteratives that occasionally are resorted to may be mentioned **calomel, colchicum, arsenic,** and **potassium iodide.** In some cases rather free action of the kidneys is desirable, and recourse may usually be had to **potassium acetate, potassium citrate,** and, in exceptional cases of more or less general eczema, to the oil of **copaiba.** Laxatives form a very important class in the treatment of this disease, as indigestion with more or less active constipation is often a striking symptom. The various **salines,** and **aperient mineral waters,** castor oil, cascara sagrada, rhubarb, and aloes, and other vegetable cathartics are useful.

In this class of cases the several digestives and bitter tonics are often prescribed with advantage, such as **pepsin, pancreatin, papoid, muriatic acid** and **gentian, quassia, calisaya,** and others.

EXTERNAL TREATMENT.—In the local management of eczematic cases soap and water must be used with judgment. In the acute and in many subacute cases these cleansing agents should be employed as infrequently as circumstances will permit.

> Washing the affected region is injurious, not so much from contact with the water as from the fact that the epithelium is deprived of the natural oil, its best protection. Toxic influences from within are an important factor, so that internal treatment is frequently necessary for a complete cure, no external measures proving permanently successful until the autointoxication is conquered. **Roentgen ray** is sometimes useful in the chronic form. W. Scholtz (Deut. med. Woch., Oct. 14, 1909).

Cleanliness may often be maintained by gently rubbing off with **cold cream, petrolatum,** or **almond oil.** Even in such cases, however, occasional washing is necessary, both for the sake of cleanliness and in order to get rid of the products of the disease and to remove the messiness which has resulted from the applications.

> When acute, weeping, erythematous eczema occurs on the face there is usually much edema in the infraorbital region, and the condition may at first be mistaken for erysipelas. Greasy applications are best avoided, and simple wet dressings with folds of butter muslin soaked in normal **saline solution,** the patient being preferably confined to his room, are most acceptable. The following **calamine lotion,** applied on lint, will relieve the irritation and smarting:—
>
> ℞ *Zinci carb.* (*impuri*) . ʒij (8 Gm.).
> *Zinci oxidi* .... ʒj (4 Gm.).
> *Glycerini* .... ʒss (2 Gm.).
> *Liquoris calcis,* q. s.
> ad .... ℥vj (180 Gm.).
> M. ft. lotio.
>
> Upon the extremities, **lead lotion** is often best; it may be combined with the calamine lotion in equal parts.
>
> When the exudation has practically ceased, powders or ointments may be applied. Of the former the **oleopalmitate of zinc** [or zinci oleostearas, N. F.] is useful. This may be mixed with one-half its weight of powdered starch. The following zinc cream is also a good application in these cases:—
>
> ℞ *Zinci oxidi* .... ℥j (30 Gm.).
> *Adipis lanæ* .... ʒij (8 Gm.).
> *Olei olivæ,*
> *Liquoris calcis,* ana
> partes æquales, ad ℥iv (120 Gm.).
>
> Misce. G. Norman Meachen (Pract., May, 1912).

A remedial application should always be made immediately after washing has been employed. In some cases, especially those of a chronic and scaly and markedly sluggish character, the use of **soap and water** is resorted to frequently and has often a therapeutic value; indeed, in some such cases the **green soap**—sapo viridis—may be occasionally or frequently used with advantage.

Applications are to be made in eczema two or more times daily, and when possible the continuous application is to be advised.

In the selection of external remedies for a particular case common sense must be employed. In those cases in which the type of disease is acute or subacute mild remedies are to be used. In the milder erythematous variety dusting powders of **zinc oxide, talc, starch,** and **kaolin** are soothing and beneficial; they may be used alone or immediately following the application of one of the washes named below. The conjoint use of **black wash** or **boric acid lotion** with **oxide of zinc ointment** or any mild ointment may give beneficial results. Or the simple oxide of zinc ointment with 20 to 30 grains (1.3 to 2 Gm.) of boric acid or 3 to 5 grains (0.2 to 0.3 Gm.) of **carbolic acid** to the ounce (30 Gm.) may be used. A compound lotion of calamine and zinc oxide, like the following:—

℞ *Calaminæ,*
Zinci oxidi ....āā ʒiss (6 Gm.).
Glycerini .... ♏x (0.6 c.c.).
Acidi carbolici...... gr. xx (1.3 Gm.).
Aquæ .... ℥vj (180 ♏.).
M.

is valuable, and may be dabbed on the surface repeatedly or by means of linen or lint kept wet with it and closely applied to the diseased surfaces, or a **boric acid lotion** with 1 or 2 drams (4 or 8 Gm.) of **carbolic acid** to the pint (500 c.c.) will be found beneficial, and especially applicable if the diseased surface is large, or boric acid (15 grains—1 Gm.—to the ounce —30 c.c.) may be added to the above calamine and zinc lotion. A so-called **salicylic acid paste,** with or without 5 to 10 grains (0.3 to 0.6 Gm.) of **carbolic acid** to the ounce (30 Gm.), is often of great advantage:—

℞ *Acidi salicylici* .... gr. x (0.6 Gm.).
Amyli,
Zinci oxidi.........āā ʒij (8 Gm.).
Petrolati .... ʒiv (16 Gm.).
M.

An ointment of **alumnol,** 20 to 40 grains (1.3 to 2.6 Gm.) to the ounce (30 Gm.) of **cold cream,** or **zinc oxide ointment** is also valuable. One containing ½ to 1 dram (2 to 4 Gm.) of **bismuth subnitrate** is also of benefit.

A compound **calamine ointment** may be used in some cases with great advantage:—

℞ *Calaminæ* .... ʒj (4 Gm.).
Amyli .... ʒss (2 Gm.).
Acidi salicylici .... gr. x (0.6 Gm.).
Ung. zinci oxidi.q s. ad ℥j (30 Gm.).
M.

Diachylon ointment, if a well-made one is procurable, is often serviceable. The soothing **salve-mulls of zinc oxide** and **boric acid** are extremely valuable in some cases.

In some cases of eczema in which the grade of inflammatory action is subacute, stronger applications may be resorted to, although even in this class of cases it is advisable to begin the treatment with the milder applications already named. These latter may finally, if necessary, be made stronger and more stimulating by the addition of **white precipitate, red precipitate, calomel,** resorcin, or tar. Of the **mercurials,** 5 to 30 grains (0.3 to 1 Gm.) to the ounce (30 Gm.) is the usual proportion called for; of **resorcin,** 5 to 20 grains (0.3 to 1.3 Gm.), and of **tar,** ½ to 2 drams (2 to 8 Gm.) of the tar ointment to the ounce (30 Gm.) of mild ointment. **Oil of cade** may also be used, ½ to 2 drams (2 to 8 Gm.) to the ounce (30 Gm.) of ointment. A tarry ointment such as the following may also prove useful in these cases:—

℞ *Liquor carbonis detergens* .... ʒss-ij (2-8 Gm.).
Cerat. simp...q. s. ad ℥j (30 Gm.).

[Liquor carbonis detergens is made by mixing together 9 ounces (270 Gm.) of tincture of soap-bark and 4 ounces (120 Gm.) of coal-tar, allowing it to digest for eight days and then filtering. HENRY W. STELWAGON.]

Crude **coal-tar** is superior as a siccative and antipruritic to all other topical applications. The writer uses it in the following manner: The surface to be treated is first thoroughly freed from crusts and scales and then carefully washed with boiled water, and if not too sensitive it is afterward soaped and wiped off with ether. The tar is then applied in a thick layer and allowed to dry for a considerable time, the longer the better, the drying being an important part of the technique. When it has dried as long as possible, not less than twenty minutes, several hours if possible, it is powdered with talc and enveloped in a soft cloth. If the skin is not too much inflamed nor the oozing too abundant, it is well not to touch the dressing for two days. If the inflammation and oozing are marked it is useful to dress the parts with a simple zinc paste the next day. After five to six days the application of the tar may be repeated. Usually 3 to 5 applications are sufficient for a cure. Brocq (Bull. de la Soc. Française de Dermat. et de Syph., No. 9, 1908).

The writer confirms Brocq's recommendation of **coal-tar** in the treatment of eczema, and uses it in the following way: The surface to be treated is washed over first with a solution of **methylene blue** in distilled water, in proportions of 1½ to 2 per cent. If a fatty excipient for an ointment containing coal-tar is desired, lanolin and vaselin are both contraindicated; fresh lard, not benzoated, on the other hand, is quite successful. To remove a layer of coal-tar which has been applied in the pure state some cotton-wool soaked in almond oil may be used. Coal-tar should not be used with acute non-weeping eczema; when vesicular, however, even though acute, coal-tar may be used with advantage. Dry, scaly, itchy eczemas do well with this treatment. Infected eczema with folliculitis or pyodermitis should be carefully disinfected as a preliminary measure. Fissured hyperkeratosic forms are not, as a rule, favorably influenced. Jambon (Ann. de derm. et de syph., Jan., 1909).

Aristol, 5 to 20 or more grains (0.3 to 1.3 Gm.) to the ounce (30 Gm.) of ointment base, may also be commended. In some instances preliminary paintings for several days with a saturated solution of **picric acid** have proved of advantage, waiting for the films or scale thus formed to come up, and then applying a mild ointment for a few days, and then resuming the picric acid painting; it should not be applied to a large surface.

In some instances applications of dressings of a more or less fixed character are of advantage, such as the gelatin dressing, tragacanth dressing, and acacia dressing.

Gelatin Dressing:—

℞ *Gelatin*	15 to 25 parts.
Zinc oxide	10 to 15 parts.
Glycerin	15 to 25 parts.
Water	50 parts.

To this may be added 2 parts of **ichthyol.**

This is heated over a water bath each time it is to be employed, a good coating painted on with a brush, and when partly dry—in one to five minutes—the parts wrapped with a gauze bandage. The whole dressing becomes dry and fixed, and may remain on from two to six days, and then soaked off, cleansed, and a new dressing reapplied. In some cases the larger quantity of gelatin and smaller quantity of glycerin may preferably be incorporated, and then the gelatin coating will dry more quickly and will form a sufficient dressing without the gauze bandage, although this latter seems to be of real advantage in keeping the gelatin from becoming soiled and from being rubbed off. If the gauze is not used a small quantity of a dusting powder may be applied over the gelatin.

The above is especially applicable

in the treatment of eczema of the lower legs. Other drugs may be added, but certain medicaments exercise an inhibitory influence on the setting of the gelatin, and if used should always be used with a dressing more rich in gelatin and with less glycerin and less water; such remedies are **resorcin, salicylic acid,** and **carbolic acid. White precipitate, sulphur,** and **acetanilide** may also be incorporated in such dressings.

Tragacanth Dressing.—Pick's tragacanth dressing—linimentum exsiccans—is also a useful fixed dressing in the cooler weather. It consists of

℞ *Tragacanth*	5 parts.
Glycerin	2 parts.
Boiling water	95 parts.

To this can be added 2 per cent. of **boric acid** or 2 per cent. of **carbolic acid,** and 5 to 10 per cent. of **zinc oxide** or **calamine,** or equal parts of both.

This is smeared in a thin coating over the diseased area and allowed to dry on, which usually requires several minutes. The parts can then be bandaged or be sprinkled with some indifferent dusting powder. It is a more simple dressing than the gelatin application, requires no preparation, but is, upon the whole, less useful. Other medicaments may be added in addition to those already named.

The best treatment for eczema labiorum or chapped lips is to apply nightly **camphor ice.** In treating chronic eczema of the hand, if the patient is not able to stop the occupation rubber gloves may be worn.

For eczema of lids and of nails the writer prescribes:—

℞ *Acidi salicylici* ..	gr. vij (0.45 Gm.).
Hydrargyri oxid. flav.	gr. ij (0.13 Gm.).
Ung. petrolati..ad	℥j (30 Gm.).

M. et ft. ung. Sig.: Apply to part after washing off crusts with olive oil.

In eczema of the legs, where we have a retarded circulation, varicose veins, the patient should elevate the legs if practicable or wear a bandage well applied. Applications of **silver nitrate** and dusting powder are useful; in stubborn cases **oil of cade** is indicated. S. Moskowitz (N. Y. Med. Jour., Feb. 13, 1909).

Acacia Dressing.—This constitutes another fixed dressing that is readily applied and which may be used on dry parts. A good formula is the following:—

℞ *Mucilage of acacia*	5 or 6 parts.
Glycerin	1 part.
Zinc oxide or *calamine,* or a mixture of both.	2 parts.

Carbolic acid or any other drug may also be added if desired.

This is painted on with a brush or smeared over in a thin layer with the finger; it dries in a few minutes. If at all sticky or for further prevention against this, a dry powder of **zinc oxide** or **talcum** can be applied over it.

Another method of treating these cases which can at times be employed with great benefit is by means of the so-called **salve-** and **plaster- mulls** (made by Beiersdorf). These are variously medicated. The mild salve-mulls and the moderately strong salve-mulls, and the moderate strength plaster-mulls are adapted for the subacute cases. While especially useful in some cases, occasionally their action is not so satisfactory. Their disadvantages are their costliness and the likelihood that they will not be found available in the shops. Especially is this the case in the country.

The writer recommends the application of the following ointment in cases of eczema of the face in children:—

℞ *Salicylic acid,*
Precipitated sulphur,
Pulverized camphor ....āā gr. xv (1 Gm.).
Oil of cade....... ʒiiss (10 Gm.).
Zinc oxide .... ʒv (¼ Gm.).
Petrolatum ...... ℥j (30 Gm.).

M. et ft. unguentum. Rostaine (Revue des hôpitaux, No. 5, 1910).

In eczema of a chronic sluggish type strong applications must be usually made before a result is brought about. The different remedies and combinations referred to in speaking of the treatment of the subacute type may be first tried; later, when necessary, treatment may assume a bolder character, various remedies being used in stronger proportion. Of value in many of these cases may be mentioned: ointments of **calomel,** 40 to 80 grains (2.6 to 5.3 Gm.) to the ounce (30 Gm.); **white precipitate** of about the same strength; **salicylic acid** ointment, 20 to 60 grains (1.3 to 4 Gm.) to the ounce; **resorcin,** about the same proportion; **sulphur,** 10 to 60 grains (0.6 to 4 Gm.) to the ounce (used at first with caution); **tar ointment,** either in official strength or somewhat weakened, or the **liquor carbonis detergens,** with **simple cerate** or as a wash, pure or diluted.

The chronic eczema of infants is a constitutional disease and must be differentiated from various forms of dermatitis that likewise affect infants. The etiology of such eczema depends upon two factors, congenital predisposition and feeding. Two forms must be distinguished, one of them the weeping eczema of the head, and the other the disseminated dry eczema. The first usually attacks well-nourished children with a pasty complexion. In addition to the hairy parts of the scalp, the regions of the ears, nose, and cheeks may be affected by the eruption. Hands and arms may likewise show the same lesions. Overfeeding and chronic constipation are the usual concomitants of this, the seborrheic form of eczema. Improvement and cure usually follow the **change** from pure **milk diet** to **mixed diet** at the **end** of the **first year.** The second variety of eczema occurs almost exclusively in artificially fed children. Such children are weak, pale, and thin. The eruption is not as strikingly evident as in the first form, and consists of scattered patches of dry, scaly, infiltrated lesions that may be found over the whole body.

While local treatment of these forms of disease must be used in every case to make the children comfortable, the cure depends not upon this treatment, but upon changes in the diet of the children. Reduction of milk is the principal point of managing these cases, and carbohydrate food must be given to make up the deficiency in the foodstuffs. After the fourth month of age this is very easy, as the child can be fed on various cereal preparations and also given fruit-juice. In later months the albumin of eggs must be avoided, as it is as badly borne as the milk proteids. Whey mixtures may be used in cases where the child is too young to take any other food but some form of milk. The whey may be modified with sugar and cereal gruel, a diet with which Finkelstein has had great success in the treatment of eczematous children. Freer (Münch. med. Woch., Jan. 19, 1908).

For old, chronic, thickened eczema plaques, the author uses **chrysarobin** or **pyrogallol** in from 1 to 10 per cent. ointments, made up with vaselin and painted on, followed by the plentiful application of **zinc** and **starch powder.** When the patches are greatly thickened they may be softened by the painting on of 50 per cent. **liquor potassæ** and then the application of 50 per cent. **silver nitrate** solution, finally to be covered with sterile gauze for one or two weeks until healed. The scab is then removed by treating with **boric ointment.** J. L. Bunch (Lancet, April 3, 1909).

An ointment of 20 to 40 grains (1.3 to 2.6 Gm.) of **pyrogallic acid** to the ounce may be cautiously tried in sluggish, thickened, obstinate cases of limited area. The same may be said with regard to **chrysarobin**; but this latter should not be used about the face. The various fixed dressings referred to in the treatment of the subacute variety will also be of value in the chronic type. **Collodion** may also be used as a basis for fixed dressing in localized areas of disease. The stronger **salve- and plaster- mulls** and the **medicated rubber plaster**, the latter especially in the sclerous and verrucous forms, are also of distinct advantage in these cases; in sluggish, thickened areas repeated **shampooing with green soap and hot water**, rinsing off, and immediately followed by a mild ointment applied as a plaster, acts admirably in some instances. Painting such areas with a solution of **caustic potash**, 1 to 5 per cent. strength, allowing it to act for a few minutes, then rinsing off, and applying a mild ointment is a somewhat similar method of treatment which is serviceable at times. In some obstinate cases thoroughly stirring the skin with a strong remedy, instituting a substitutive inflammation, and then applying mild remedies will not infrequently bring about the desired result. Finally, in persistent cases recourse may be had to the use of the **high-frequency, flat vacuum electrode**, and to the cautious employment of the **X-ray.**

The writer successfully treated with the **quartz lamp** 12 cases of eczema of various types, which had resisted all other methods of treatment. It should be tried in obstinate, recurring vesicular, eczemas which have failed to respond to other forms of treatment, including the X-rays; in pustular eczemas of the scalp and beard to prevent relapses; and in chronic eczemas with infiltration, of the psoriasiform type, for the removal of the infiltration. Rave (Archiv f. Dermat. u. Syphilis, Bd. ci, Heft 1, 1910).

The writer recommends **venesection plus saline infusion** in the treatment of skin diseases. This "lavage of the organism" washes out toxins. It withdraws 100 or 200 c.c. (3⅓ to 6⅔ ounces) of blood from a vein and then infuses without removing the cannula 300 or 700 c.c. (10 to 23⅓ ounces) of a 0.9 per cent. salt solution, repeating this from three to six times at intervals of five or six days. No by-effects to cause uneasiness were observed on the part of the kidneys or vascular system in any case, so that he does not hesitate to apply this treatment even to the elderly, up to the age of 73. No fever was observed, and the technique can thus be applied to out-patients. The best results were obtained in pruritus, urticaria, furunculosis and eczema. Simon (Deut. med. Woch., Nov. 30, 1911).

The writer has the patient expose the part affected in the heat from an oven or other source at a temperature of 100° or 115° C. (212° or 239° F.), passing the part gently back and forth five or six times until the prickling from the heat has stopped, doing this two or three times and repeating it three times a day at first. The part should be held closer to the source of the heat each time, and the patients do this instinctively when they feel the relief from itching and the benefit generally from the process. After the dry exposure a folded towel is dipped in boiling water and laid gently on the part and moved to and fro, applying this with more force each time. Patience and perseverance were necessary to conquer the old chronic eczema in the case reported, the writer himself being the victim, but permanent success finally crowned his efforts after a number of relapses. The cleanliness, simplicity and self-regulating features of the method and its prompt relief of the distressing symptoms are the special advantages of this combination of **heat and boiling water.** The only drawback is its tediousness. In his case the eczema previously kept constantly recurring and extended from the top of the head to the toes. Toth (Jour. Amer. Med. Assoc., from Berl. klin. Woch., Oct. 7, 1912).

The writer used applications of heated air in 35 cases of eczema in infants, with good results. Most of the cases had already been treated with ointments and zinc oxide pastes without success. Under the **hot-air** treatment the little patients gained in weight, the itching diminished, and the lesions disappeared in a relatively short time. The treatment was applied for five to ten minutes, once daily, and in the intervals the affected region was covered with olive oil. Strict dietetic measures should be enforced during the treatment. J. Perlmann (Münch. med. Woch., Jan. 9, 1912).

In infants the face and scalp are by far its most common sites. The disease may, however, occur upon any part at any age. The treatment in regional eczema is essentially the same as the treatment of eczema of any part, common sense suggesting selection or avoidance which the character of the region may suggest; as, for instance, upon hairy parts, as the scalp. Ointments containing large percentages of pulverulent substances, such as the so-called salicylic acid paste, should not be employed, as they would tend to produce crusting, matting, and messiness.

In the eczemas of children we must constantly keep in mind a feature that distinguishes these forms from those occurring in adults, namely, their intimate connection with disturbances of metabolism. Purely local treatment is in most cases successful in the case of adults, very seldom in the case of infants.

It is rather apt to be a well-nourished, healthy appearing infant that is the subject of the common type of infantile eczema which begins usually on the cheeks or scalp, and often sparing the parts about the nose and mouth, extends to the whole head and face and often persists for several years. When this form of eczema spreads to the body, it usually assumes the form of a papular eczema at first, later, perhaps, becoming moist. This form of eczema is especially common in breast-fed infants and in those that are well nourished, as has been said. The writer believes that whether well nourished and apparently robust or not, these infants are subject to gastrointestinal disturbances which are caused by improper nourishment. Pick (Wiener med. Woch., Sept. 25, 1909).

Under the **thyroid** treatment there is usually an acute exacerbation, which gradually subsides. At the end of two weeks the skin condition is improved, and about a week later the eczema is cured or greatly attenuated. In a few instances the disease seemed to be aggravated by the thyroid. The drug should be reserved for sluggish cases, when the eczema has resisted ordinary measures, including the dietetic and hygienic. No untoward effects were ever noted, though it was used in a large number of cases and in some of them over long periods. The thyroid treatment was found useful in fat babies with an inherited rheumatic taint, in whom the "arthritic diathesis" is likely to be accompanied by thyroid insufficiency. C. Rocaz (Annales de med. et de chir. enfant., Nov. 1, 1910).

Infantile eczema is not primarily a disease of the skin, but is a cutaneous symptom of some internal disorder. Treatment directed toward the skin disturbance will be of little avail unless the basic internal disorder be at the same time corrected. For the early erythematous eruption about the face use a lotion as follows:—

℞ *Acid. carbolic.* .... gr. x (0.6 Gm.).
Magnes. carb.,
Zinc. oxid.......āā ʒj (4 Gm.).
Glycerini .... ʒss (2 Gm.).
Aq. calcis .... ℥ij (60 c.c.).
Aq. dest. ....ad ℥iv (120 c.c.).

Applied two or three times a day, with the conjoint use of a mild **sulphur** and **salicylic ointment** on the scalp to combat the seborrhea, this will be found usually sufficient if the toxic disturbance be also corrected. If extensive weeping or oozing surfaces be present nothing is so effective and soothing as wet compresses of **liq. plumbi subacetatis,** a dram (4 Gm.) to a pint (500 c.c.) of cold water, applied for twenty minutes three or four times a day, and followed by the lotion above mentioned. In cases of some duration tar is the most effective remedy, and may be used as in the following formula:—

℞ *Acidi carbolici,*
Acidi salicylici...āā gr. iij (0.2 Gm.).
Ung. picis liq...... ʒj (4 Gm.).
Lassar paste.....ad ℥j (30 Gm.).

This is applied in a thick layer over night, and removed in the morning, and the magnesia lotion kept on during the day. A. J. Markley (Pediatrics, Nov., 1911).

Henry W. Stelwagon,
Philadelphia.

EDEMA. See Ascites and Edema.

EDEMA, ANGIONEUROTIC. See Ascites and Edema.

ELATERIUM AND ELATERIN.—Elaterium is a sediment deposited from the juice of the squirting cucumber (*Ecballium elaterium,* A. Rich). This sediment, when dried, appears in friable cakes about 1/10 of an inch in thickness, flat or slightly curled, and of a pale-green, grayish-green, or grayish-yellow color, the yellow tinge appearing when the drug is old. Its odor is feeble and its taste bitter and slightly acrid. It is slightly soluble in alcohol, ether, chloroform or benzene, but insoluble in water. *Elaterin* (elaterinum—U. S. P., B. P.) is the neutral principle of elaterium, being found therein in amounts varying from 5 to 40 per cent. It is a neutral principle and appears as small, white, or yellowish-white crystals, without odor, but of a very bitter and acrid taste. It is freely soluble in chloroform, slightly soluble in ether and alcohol, and insoluble in water. Elaterin is preferred for administration because of the great variability in strength of different specimens of elaterium.

PREPARATIONS AND DOSE.—*Trituratio elaterini,* U. S. P. (trituration of elaterin) is composed of 10 parts elaterin and 90 parts sugar of milk. Dose, gr. ½ (0.030 Gm.). *Elaterin* is given in the dose of 1/10 gr. (0.005 mg.).

PHYSIOLOGICAL ACTION.—Elaterium is a decided irritant to the mucous membrane and also to the skin, and frequently causes ulceration of the fingers and eyes in those working with it. When given internally its chief action, in man, is to produce profuse, watery stools. It is said that this drug also produces a purgative effect when applied externally. Small doses act as a stimulant to the mucous membrane of the stomach and intestine, increasing their secretions. It is also said to act as a stimulant to the liver and pancreas. When given in proper doses, these large, watery evacuations occur without undue pain or any apparent gastrointestinal irritation, and for these reasons elaterium claims first rank as an hydragogue purge.

POISONING BY ELATERIUM.—In large doses or in debilitated persons its use may produce so much prostration and exhaustion as to demand the exhibition of stimulants and other supporting measures. In addition to nausea, vomiting, excessive purging, and exhaustion, the use of too large doses of this drug may even be followed by death from gastroenteritis. Debility from old age or other cause and gastrointestinal irritation or inflammation contraindicate its use.

The subcutaneous use of elaterium, although capable of producing catharsis, is not advised, on account of the severe local irritation and inflammation thereby induced.

TREATMENT OF ELATERIUM POISONING.—The treatment of poisoning by this drug is practically that of gastroenteritis. **Morphine** should be given hypodermically, and **hot applications** (stupes or flaxseed poultices) should be made **over the abdomen** to allay the pain and control the irritation and diarrhea. Especial care should be had in the selection of a proper **diet.** Bland, easily digested, and unirritating articles of food should be selected. Predigested foods are especially useful in these cases.

THERAPEUTICS.—Elaterium has been used in conditions demanding depletion, but salines are usually preferable in such cases; the use should not be continued if the stomach becomes disordered or the appetite impaired. It should never be used in cases of debility or marked exhaustion, and may be followed with advantage by alcoholic stimulants soon after its action is manifest. Its use is suggested in **cerebral congestion** on account of its depletant and derivative action. In **poisoning by narcotics** and in **acute alcoholism** elaterium is indicated when the emunctories are not acting freely.

It should not be used in cases of ordinary constipation, on account of its violent action. It is also contraindicated in inflammation of the stomach and intestines, in extreme exhaustion, any weak heart condition, and during pregnancy.

In **ascites** and **dropsical effusions** elaterium is of great value, though one the use of which demands much care and judgment. In dropsy depending on **aortic, obstructive,** or **regurgitant disease** it is especially useful, given in small doses at first, beginning with gr. 1/20 (0.003 Gm.) and increasing the dose on alternate mornings at say 5 o'clock, so that its action is finished by noon. This is claimed, by Hyde Salter, to quiet the heart, relieve the dyspnea, lessen the pulmonary congestion, and diminish the hydrothorax.

Uremic poisoning is much benefited through the use of elaterium, as it aids the elimination of the uremic poison by the bowel. It is especially indicated when uremia is associated with dropsical effusion.

In **pulmonary edema, pleurisy,** and **pericarditis,** the hydragogue catharsis induced by elaterium sometimes proves beneficial.

S.

ELECTRIC CHOREA. See Chorea.

ELECTROTHERAPEUTICS.—While electricity has long been used in the treatment of disease, and inventions in appliances for electrotherapeutics are in some measure commensurate with those used for industrial purposes, the use of electricity in medicine is still largely discredited or ignored by a considerable portion of the medical profession. Several factors have contributed to the production of this condition of affairs, prominent among which has been the disappointment caused by its failure to produce impossible results which were previously expected of it. The reaction from this disappointment was accentuated by the fact that irregular practitioners have continued to exploit it and claim for it obviously unreasonable powers. Many medical colleges have only the most perfunctory courses in electrotherapeutics, or some none at all, and medical graduates frequently start in practice with little knowledge of the physics of electricity, and less of its physiological effects when applied to the living body in the various modalities. So it has come to pass that electricity is considered by many to be useful in any large degree only to the "quack," or to have its chief value in the psychic effect produced by its use. It is much to be regretted that so much emphasis has been placed on the so-called "psychic" effects of the various applications of electricity. Not only is the scientific knowledge of the physiological and therapeutic effects of the different modalities sufficiently established to justify their rational application for specific results, but the modern status of psychotherapy does not justify the blind and indiscriminate use of a force which is mysterious, not only to the patient, but too frequently to the physician applying it.

Electricity has undoubtedly a very distinct and rather wide field of usefulness as a therapeutic agent, but one which can be successfully utilized only when its properties, physical as well as physiological, are well understood. Although the limits of this chapter prohibit a detailed presentation of the subject of electrophysics, certain fundamental considerations of this phase of the subject are required.

GENERAL CONSIDERATIONS.—*Nature of Electricity.*—As is the case with all of nature's forces, an ultimate knowledge of electrical force is lacking; it is only known by its manifestations, and from these certain rules or laws have been formulated. By means of these laws are explained the relationship between the different forms or currents of electricity, and the fact that all of these different forms are essentially the same force manifesting itself in different ways according to the source by which it is generated or the influences to which it is subjected. And by practical utilization of these laws it is possible not only to regulate and measure the currents applied, but also to have available from a single source several currents having different properties.

Electric Potential.—The character of an electric current is determined largely by its potential, that is, its ability to overcome resistance. There are many analogies between hydrostatics and electrodynamics, and just as the force with which water flows from an opening in a pipe depends on the pressure of water within the pipe, so the potential of an electric current depends upon the pressure or "voltage" of its source of supply. As with water, the smaller the opening in the pipe the less is the actual amount that escapes with a given pressure, so with electricity the greater the obstacle to its passage the smaller the amount of the current which passes through a conductor with a given voltage.

Resistance and Intensity of Current.—Although electricity is capable of traversing in some degree all kinds of matter, some materials, such as glass, amber, rubber, etc., offer enormous resistance to the current, and are called non-conductors, or insulators; other materials, as metals, and especially copper, offer very little resistance, and are called conductors. But all conductors offer a definite amount of resistance which varies directly with the length of the conductor and inversely with the area of its cross-section. As will be readily seen, the amount of the current passing through a conductor will depend on two factors, viz., the potential and the resistance, varying directly with the former and inversely with the latter. The units in general use for measuring the potential, the resistance and the amount of the current are, respectively, the volt, the ohm, and the ampère. One ampère represents a definite amount of force passing through a circuit; it is a unit of intensity. An ohm represents the resistance offered to an electric current equivalent to that of a column of mercury with a cross-section of 1 sq. mm. and 106 cm. long; and a volt represents the potential necessary to force 1 ampère of current through the resistance of 1 ohm. From this is formulated Ohm's law, which is $C = \frac{E}{R}$, or, transposed, $E = CR$, and $R = \frac{E}{C}$, in which C = current in ampères, E = potential in volts, and R = resistance in ohms. A thorough comprehension of the application of Ohm's law is essential to a working knowledge of electrotherapeutics as well as any other branch of electrical science.

Polarity.—Electricity, whether in motion or at rest, manifests two opposing states—a positive and a negative—which tend to mutually neutralize each other. If an electric current could be said to have any direction of flow, it may be conceived as passing from the positive to the negative states or points in a circuit. As will be considered later, in certain currents the effect of this polarity is lost by reason of its rapid alternations in a given circuit.

The constant or direct current is a current in which the flow of electricity through the conductors is smooth and continuous, the polarity remaining fixed. Medically it is used only in small amounts, the 110-volt D. C. commercial current (generated by dynamo) being adequate for nearly all purposes in which the constant current is useful. A battery of from 40 to 60 cells, or a storage battery, may be used to furnish this form of electric force, which is also called "galvanic" or "voltaic" electricity. In the application of the direct current the intensity is regulated by a rheostat, by means of which a varying amount of resistance is interposed in the circuit and the ampèrage correspondingly reduced. As the intensity of current required for medical purposes is so small, the unit of measure employed is the milliampère, which is $\frac{1}{1000}$ of 1 ampère, and the milliampèremeter is the instrument which records the amount being used.

The alternating current, so largely used for commercial purposes, is generated by dynamos, and is characterized by a rapid succession of alternations in the polarity or direction of flow of the current, usually 60 cycles (120 alternations) per second. This current is unsuitable for many uses to which the direct current is applicable, but has special uses of its own, and is readily transformed to any desired potential. It is the standard commercial current where electricity is transmitted long distances.

Induced Currents.—By induced electric currents are meant those which are produced in circuits which have no direct or metallic connection with the source from which they are derived. If the conductor or wire of a circuit carrying a direct current is closely parallel to part of another circuit having no independent source of supply, each time the flow is interrupted or started in the first circuit momentary waves of electricity are induced in the second circuit. This impulse in the second circuit is in the opposite direction to that in the first when the current is started, but flows in the same direction as the first when the latter is interrupted. One of the simplest applications of this principle is the faradic coil. In this instrument a small coil of wire, the "primary" coil, in connection with a direct current is surrounded by, but has no metallic connection with, a larger "secondary" coil. A vibrator, or mechanical interrupter, in the primary circuit causes the make and break with any desired rapidity. This induced current in the secondary coil is the faradic current, and is accentuated if a core composed of a bundle of soft-iron wire is placed within the primary coil. The potential or voltage of the induced or secondary current depends upon that of the primary circuit and the relative number of turns in the windings of the two coils. Thus, if the number of turns in the two coils be the same, the voltage in the induced is the same as that in the primary current. However, the induced current is an alternating one, the rapidity of the alternations corresponding to the rapidity of the make and break in the primary by the interrupter, and it should be stated that the impulse caused by the break is greater than that induced by the make in the primary, thus producing a certain amount of noticeable polarity in the secondary circuit. If the number of turns in the secondary is double that of the primary, the voltage is doubled, and so the voltage of the secondary circuit can be regulated at will; but with each increase in voltage there is a corresponding loss of intensity in accordance with Ohm's law. In the large Ruhmkorff coils used in X-ray work the secondary windings contain many miles of fine, carefully insulated copper wire.

The principle of induction is also utilized in transforming commercial alternating currents to any desired potential, high or low, by means of "step-up" and "step-down" transformers.

Static Electricity.—Static, franklinic, or frictional electricity is electric force manifested in very high potential and low intensity, but differs from induced currents of similar high voltage and small volume in having a fixed polarity, whereas the induced current is of alternating polarity. The voltage of static currents cannot be accurately measured, but is estimated by the length of the spark discharge to be hundreds of thousands of volts for the larger machines. The ampèrage of this current, even from the most powerful machines, attains only 8 or 10 milliampères, and from the average 24 glass-plate machine 1 or 2 milliampères.

High-frequency Currents.—This designation applies to several currents which vary as to the potential and the ampèrage, and signifies electric currents of generally high potential of an oscillating, alternating polarity of inconceivable rapidity estimated at from 500,000 to several million oscillations per second. The principle of their formation is essentially that of a series of step-up transformers or induction coils with which are utilized condensers or Leyden jars. The rapid discharge through the spark-gap of the secondary circuit also represents the discharge of the condensers. Each discharge of these is accompanied by thousands of oscillations of alternating polarity which are transmitted to coils or "solenoids" of different types and arrangements. Of the high-frequency currents used therapeutically there are two principal types, viz., the d'Arsonval and the Tesla, or Oudin. The d'Arsonval current is of comparatively low potential and high ampèrage, the latter reaching a maximum of 2000 or 3000 milliampères. The Tesla and the Oudin currents are essentially the same, and have a potential approaching that of the static current, but differ in having an alternating character, whereas the static is of fixed polarity. It is the Tesla type of current that is utilized for the production of Hertzian waves in wireless telegraphy.

THERAPEUTICS.—Galvanic currents for medical use are derived either from batteries or commercial circuits. The necessary apparatus for the control and application includes a controller in the form of a rheostat of a potential reducer, a milliampèremeter, a pole-changer, and various electrodes. These can be conveniently arranged in a portable box if a battery is used, or on a table or cabinet. The potential of the source of supply may be from 50 to 110 volts, but must be completely under control so that any desired amount of current, even 1 or 2 millampères, may be applied smoothly; otherwise, undesirable and painful shocks are produced. Since the positive and the negative poles produce different effects, it is always necessary to bear in mind the polarity of the current. By means of the pole-changer, the polarity of the electrodes may be reversed without changing their position. The electrode having a positive polarity is called the anode, the one with the negative being the cathode. The amount of current used in therapeutics varies from 1 to 200 milliampères, but few operators find it advisable to use more than 50 to 60 milliampères.

An important characteristic of the galvanic current is its power to stimulate muscle to contraction when applied either to the motor nerve or to the muscle itself; with small currents, contractions occur only when the circuit is made or broken, and in the normal condition are momentary and followed by immediate relaxation. The force of the contractions vary with the strength of the current, and also according to whether the anode or the cathode is applied to the muscle or nerve, or whether the circuit is made or broken. In cases of lesion, or disease of the peripheral motor nerves, or of the motor cells from which they originate in the spinal cord (or brain-stem in the case of cranial nerves), certain changes take place in the character of the reactions which are known as the reactions of degeneration (R. D.). To test the electrical reactions of muscles, one electrode is applied to the part to be examined, the other at some indifferent point. The electrodes should be covered with cotton or felt and moistened with a weak solution of sodium bicarbonate. By the pole-changer the electrode on the part examined is made the cathode, and starting with the current at zero the rheostat is gradually regulated to slowly increase the current; at the same time alternately opening and closing the circuit by means of a breaker in the handle of the electrode. When the first contraction occurs in the muscle, note is made of the reading of the meter, and whether it occurs at the make or the break. Continuing the same way the current is increased until contractions occur both at the make and the break, and the number of milliampères is again noted. Reversing the pole-changer so that the active electrode becomes the anode, the procedure is repeated, after which the record shows the minimum current strength necessary to cause contractions with the cathode and the anode when the circuit is opened and when it is closed. The following formula expresses the normal reactions: $\mathrm{CaClC} > \mathrm{AClC} > \mathrm{AOC} > \mathrm{CaOC}$, which signifies that the cathode-closure contraction is greater (or occurs with smaller current) than the anode-closure contraction, which is greater than the anode-opening contraction, which, in turn, is greater than the cathode-opening contraction. During the degeneration of a motor nerve and the atrophy of the muscle, beginning about ten days after an injury, both the reaction formula is changed and the character of the muscular contraction is altered. The excitability of the nerve is diminished or lost, that of the muscle is increased at first and later diminished, and the contraction itself becomes slower and extends through the muscle in a wave-like motion. The reaction formula changes, the minimum contraction occurring at the anode, as AClC>CaClC>AOC>.CaOC or AClC>CaClC>CaOC>AOC. With the faradic current reactions of degeneration are only manifested in a quantitative change, *i.e.*, contractions diminish in strength or disappear and gradually return with regeneration.

The reactions of degeneration are not only valuable in diagnosis, but also in prognosis, as the amount of change in the responses is an accurate indication of the degree of injury to the nerve. In a case of Bell's palsy, in which the paralysis of the facial nerves is complete, the presence of faradic response and only slight galvanic R. D. ten days after the onset indicates rapid and complete recovery; loss of faradic contractions and reversals in the galvanic formula in a similar case would indicate slow and probably incomplete recovery.

The ability of the galvanic current to produce contractions in paralyzed muscles when all other measures fail makes it an important therapeutic agent for stimulating the nutrition and circulation as well as the regeneration of the affected nerves in **peripheral neuritides, acute poliomyelitis,** and allied conditions. Applications are made in the same manner as described in testing the reactions, using current sufficient only to cause contractions and frequently opening and closing the circuit. It is seldom necessary to use more than 10 or 15 milliampères of current for this purpose, and daily applications should employ but a few contractions for each muscle.

Cataphoresis.—It has been demonstrated that medicinal substances in solution on an absorbent electrode can be forced by the galvanic current into the living tissues, or even entirely through them, appearing in the opposite electrode. This has given rise to the method of administering various medicaments called cataphoresis, for the reason that most of the substances so employed are attracted by the cathode pole. It should be noted, however, that such substances, including the metals, bases and alkaloids to be absorbed, must be applied at the anode, for the reason that they are electropositive, such as acids, acid radicals, and also the halogens, electronegative substances, are applied at the cathode. Cocaine applied to a body surface (anode) produces superficial anesthesia. Solutions of magnesium sulphate by cataphoresis have been employed with success in the treatment of **flat warts,** but were unsatisfactory for the fungating type. Urethral cataphoresis, using a ½ per cent. solution of zinc sulphate, has been reported by Bouchet (1907) to be valuable in the treatment of **acute** and **chronic gonorrhea.** Salicylic cataphoresis with a 10 per cent. solution of the sodium salt at the cathode relieves the pain of **myalgias, neuralgias,** and some forms of **rheumatism** when applied over the affected area.

The current strength employed in cataphoresis is usually small, being limited by the toleration of the patient. Large electrodes allow stronger currents to be used than small ones. Massey applies the term "mercuric cataphoresis" to his method of treating **neoplasms**, but it is really a combination of cataphoresis and electrolysis, since not only is mercury deposited in the tissues, but also destruction of tissue takes place by action of the electricity. This method is employed under general anesthesia. Several zinc needles amalgamated with mercury connected with the anode are thrust into the tumor and the current is very gradually increased to 100 or even 200 milliampères, according to the effect desired. The result is a destruction of the tissue about the needles, with gradual separation of the slough and healing by granulation. The technique for this operation is important, as a sudden change of potential while the heavy current is passing would be dangerous. The indifferent electrode is very large and covered with wet clay, or kaolin.

Electrolysis.—One of the manifestations of the galvanic current is the decomposition into their constituent elements of substances through which it passes. This is exemplified by the liberation of hydrogen and oxygen at the surface of electrodes submerged in water, H from the cathode and O from the anode. When galvanism is applied to living tissues by means of needles or small electrodes, local electrolysis occurs amounting to necrosis if the application is sufficiently strong or prolonged. The action differs at the two poles, that at the anode having the character of an acid burn, that at the cathode of a caustic alkali. The electrolytic action of electricity is adapted to the removal **of superfluous hair** and the destruction of various small **warts, nevi, sebaceous cysts**, etc.

In this form of application small potential is required, about 10 volts usually being sufficient, and a few dry cells or a storage battery answer very well. A volt-controller should be used if the 110-volt industrial current is utilized. A rheostat and meter are also required. Gold or iridoplatinum needles are advisable, since steel ones are attacked by the chemical action of the fluids liberated. Either unipolar or bipolar applications may be employed. In the former the indifferent electrode may be held in the hand of the patient. In bipolar applications two needles attached to one handle are insulated from each other and each is attached to one of the poles of the circuit.

In **removing superfluous hair**, unipolar electrolysis is used, and, with no current flowing, the needle, connected with the negative pole, is very carefully inserted alongside the hair directly into its follicle to the bottom. The current is slowly turned on, using from 1 to 3 milliampères of current. A slight froth appears around the needle, and there is always some discomfort or pain connected with the operation. Cocaine cataphoresis may be utilized on the surface treated, for the comfort of the patient. Hairs close together should not be selected for a single treatment, as soreness or scarring is likely to result, and in any event slight soreness and redness may last for a few days and minute temporary pitting occur.

For the removal of warts and **moles**

the cathode needle is thrust through their structure near the base; the current of about 10 milliampères is then passed until the surface is blanched. Two or more needles on one electrode are used if the wart is large. The same precautions are employed in turning the current on and off as with all other treatments by electrolysis,—the electrodes should not be applied nor removed while the current is turned on. For **nevi, port-wine stains,** etc., bipolar electrolysis is employed.

In the treatment of urethral stricture by electrolysis the object is not to destroy tissue, but only to soften the constrictions by the cathode current to the point of making them dilatable. For this purpose Newman's olivary urethral bougies with insulated stems are employed, and when in place against the stricture a current of about 5 milliampères is turned on, at the same time making gentle pressure until the bougie passes through the constriction. The size of the bougie to be selected should have only slightly greater diameter than the caliber of the stricture. Treatments may be given at intervals of about one week.

For **esophageal strictures** of traumatic or caustic origin treatment similar to that for urethral strictures may be employed with success.

Galvanocautery.—Either the direct or alternating current may be utilized for the galvanocautery, which depends upon the heating to incandescence the platinum electrode by the passage through it of a current of heavy ampèrage, but small voltage. From 10 to 20 ampères are required for ordinary work, and this can be obtained from a 6-volt current if the resistance is sufficiently low. Similar ampèrage from high-voltage currents is wasteful of energy and dangerous to use. The source of current may be either bichromate cells or storage battery wired in series parallel; or where the commercial 110 volts D. C. is utilized, a combined motor and generator which delivers current of low voltage is advisable. Suitable current for galvanocautery is readily obtained from the commercial 110 volts A. C. current by means of a step-down transformer. The galvanocautery is applicable where actual cautery is needed, electricity playing no part in the application.

The Faradic Current.—A faradic coil may be operated by direct currents of from 4 to 110 volts. Even a single voltaic cell will furnish sufficient current to cause powerful muscular contractions and painful sensations. The high voltage of the street current (110 volts D. C.), when regulated by resistance (rheostat), works satisfactorily, but the strong sparking at the interrupter rapidly burns out the platinum contact points. A volt-controller may, therefore, be used with advantage to reduce the current to about 6 volts. The commercial alternating current will operate a faradic coil, but the result is unsatisfactory, as the induced current from it is very jerky and uneven. Various forms of apparatus have been suggested to convert the alternating current directly into the galvanic, but though the so-called converters may work fairly well for a time, they deteriorate, get out of order and need renewal, and are generally a nuisance. Where only the alternating current is available, the only practicable way of obtaining dependable galvanic electricity for the faradic coil, as well as for other uses, is by means of the motor-generator, a combination of motor operated by the alternating current connected with a dynamo which generates the direct current.

The chief effect of the faradic current is its power to cause muscular contraction. With a vibrating interrupter the electric impulses are so rapid as to produce a tetanic contraction of the muscles to which it is applied; when the interruptions are slow, individual momentary contractions are produced. When a motor nerve is degenerated, the muscles it supplies lose their irritability to the faradic current, as was mentioned in discussing the reactions of degeneration.

By virtue of its property of causing muscular contractions, the faradic current is widely applicable in stimulating **weak, paretic** or **paralyzed muscles,** and by general application and by means of baths for its tonic effect.

On the sensory system, rapidly interrupted mild currents cause a rather pleasant, soothing sensation of vibration, but stronger currents, especially when applied with a wire brush or a pointed metal electrode, give rise to severe pain. Thus, by its sensory effect, the faradic current may be utilized either as a sedative or as a stimulant or counterirritant. Applied at the site on **neuralgias** with a strength moderately painful for from five to ten minutes, much relief is often obtained.

Static Currents.—The true static current can only be obtained in sufficient amounts for therapeutic use from the static or influence machine, which consists of a series of insulated glass, mica, or fiber plates revolving rapidly in close proximity to other similar plates. The electricity is delivered at the terminals in the form of currents of exceedingly high voltage, but low ampèrage and fixed polarity, and which will pass in sparks between the poles through many inches of air space. The static machine is operated by an electric or water motor, and should be inclosed in an air-tight case to exclude moisture, which will prevent its working. In prolonged wet weather, or in damp locations, the static machine may refuse to charge in spite of all precautions. It is well to keep within the case several dishes containing about 10 pounds of well-dried calcium chloride, which should be dried again as often as it becomes soggy with moisture. Much heat is required to dry this substance on account of its attraction for water. For quick starting in emergencies, a 4-quart pail filled with equal parts of chopped ice and salt hung from a hook in the top of the case, or placed on a dinner plate on the bottom, can usually be depended upon. Large quantities of water condense and freeze on the surface of the pail, which must be removed before the frost melts. The case should be opened and closed quickly. A hygrometer within the case is of value in indicating the humidity and the efficiency of measures used to reduce it.

The output of a machine in good working order is determined by the number and size of the revolving plates and the speed at which they are run. There are several different forms in which static electricity may be applied therapeutically, depending upon the manner in which the patient is connected with the apparatus, and are divided into three types, the disruptive (sparks), the convective, and the conductive.

Disruptive discharges, or static sparks, are administered by placing the patient upon an insulated stand to which the positive pole of the machine is connected. With the opposite pole grounded, the sliding rods of the spark-gap are separated beyond the sparking distance, and the patient's body is approached with the ball electrode with a chain attached reaching to the floor. The electricity passes in sparks between the patient and the electrode, and their size can be regulated by the speed of the machine, or by the more or less complete grounding of the electrode and of the negative pole of the machine. The strongest possible sparks are obtained by connecting the electrode by chain with one pole of the machine and the insulated table with the other. This method of application is more or less disagreeable, and sparks should not be drawn from sensitive areas nor from bony prominences on account of the pain produced. The effect of the static spark is to cause a momentary muscular contraction, a sharp or sometimes pounding sensation, and a small point of irritation on the skin for each spark contact. Repeated sparking at one small area will produce vesication. Static sparks are applicable principally in localized muscle spasms and myalgias, to cause contractions of atonic muscles, and to produce reflex effects.

The *convective discharges* include the "static bath," "static insulation," and the various "breeze," "spray," and "brush" discharges. The arrangement of the patient is the same as for the sparks except that either no electrode at all is used or only such as cause no spark, as pointed metal or those of material having great resistance, such as wood, etc. Static insulation, or static bath, may be either interrupted or constant; in the former case the spark-gap is reduced until sparks pass causing the patient's body to be alternately charged and discharged with varying rapidity. When continuous, the spark-gap is widened and the patient is constantly charged with electricity which escapes into the air. The breeze, spray, and brush discharges are modifications of static insulation, grounded electrodes of pointed metal (for breeze and spray) or wood being held near to the patient, causing a rapid escape of electricity, which gives the sensation of blowing air, warm or cool, or of hot sand in the part which the electrode approaches.

Static insulation gives the patient a mild, pleasant sensation, often relieving headache and producing drowsiness. The spray and brush discharges are mildly stimulating to the skin, relieve pain, and promote the healing of sluggish wounds and ulcers.

The *conductive discharges* include the *static induced currents* and the so-called "wave currents." For the production of the static induced current, each pole of the machine is connected with the inner armature of a Leyden jar, the outer armatures being the source of the induced current. With each discharge at the spark-gap the inner coatings of the Leyden jars are charged and discharged, producing oscillations of a to-and-fro character in the outer coatings. Electrodes connected with these give a current having much the character of the faradic current, *i.e.*, rapidly alternating and of high potential, and its strength depends upon the size of the jars, the speed of the machine, and the length of the spark-gap; there is, therefore, a very wide range of adjustment. The patient is not insulated in applying this current. The therapeutic application is practically the same as that of faradism.

The *wave currents,* typified by the Morton wave, were so named because in its application Hertzian waves emanated from the patient. The connections for this current are made, after closing the spark-gap by moving the sliding rods, by placing the patient on the insulated platform, grounding the negative pole of the machine, and applying the positive electrode directly to some cutaneous surface. On separating the sliding rods, the patient's body will be charged with positive electricity, which escapes with each discharge of the machine through the spark-gap; it is by regulating the length of the sparks that the effects are controlled —the longer the sparks, the more powerful the effect. For the more vigorous treatments the skin contact should be large, using metal plates of molding tin, or lead-foil, to the body surface to be treated; strong currents through small skin contacts cause disagreeable muscular contractions, and separation of the electrode from the skin surface causes very painful sparks.

The effects of the wave currents are local and general. The local effect is manifested mainly in muscular contraction, varying in degree and extent according to the length of spark and the area of electrode and skin contact. The frequency of contraction varies with the rapidity of the spark discharge. The general effects consist of a sensation of vibration throughout the body, and are said to counteract **deficient metabolism** and reduce **high blood-pressure.** The wave current is a very desirable means of causing muscular contractions, as the effects are powerful and penetrating and practically painless if the electrode is sufficiently large. Hence its reputed value in **muscular atony.**

Static high-frequency currents are derived from accessory apparatus, as the solenoid or resonator, connected with the poles of the static machine, and will be considered later.

High-frequency Currents.—As has already been stated, high-frequency currents are essentially characterized by high potential and inconceivably rapid oscillations of alternating polarity, which is made possible by the discharges from condensers or Leyden jars. Almost any source of electric supply may be utilized for the production of high-frequency currents, but with varying degrees of efficiency. When the direct or galvanic current is used, a Ruhmkorff or X-ray coil may be employed. With this apparatus the primary circuit is interrupted by a mechanical or electrolytic interrupter, and the terminals of the secondary circuit connected with two condensers. The opposite sides of the condensers are connected with the extremities of a coil called the d'Arsonval solenoid, with which is also associated another (the Tesla) coil, or the Oudin resonator. When the alternating current is used, it may be converted into the direct current by means of a motor-generator and utilized as above, or may be directly transformed into a high-potential current by means of a step-up transformer, the secondary terminals of which are connected with condensers and solenoid. In this arrangement the alternations of the primary current serve as interruptions and the mechanical or electrolytic interrupter is not employed. In each of the above arrangements an adjustable spark-gap in the secondary circuit discharges the condensers and regulates the voltage and frequency. With the static current the poles of the static machine are connected with the condensers, and these with the solenoid, as previously described.

The currents of high frequency are of oscillating, alternating character, and vary in potential and ampèrage according to the source of original supply, and also according to the terminals employed. The static high-frequency currents have the smallest ampèrage, registering only a few milliampères, while the transformer apparatus furnish d'Arsonval currents of 2000 to 3000 or more milliampères.

For rendering available the different modalities, or types of current, terminals are placed on the apparatus connected with the various coils. Thus, the two terminals of the secondary winding furnish a modified faradic current having high potential, the thermofaradic. Connections with the extremities of the d'Arsonval solenoid furnish the d'Arsonval current, which is of comparatively low potential and high ampèrage. Usually only one terminal of the Tesla coil or Oudin resonator is employed, and the current from this is of very high potential, but low in ampèrage.

Effects of High-frequency Currents.—It is to be noted that there are marked differences characterizing the action of high-frequency currents as compared with other electric modalities. In the first place the electrolytic action, so prominent in the galvanic current, is entirely lacking in the high-frequency, its energy being expended in generating heat rather than chemical effects. A high-frequency current that will not discolor a solution of potassium iodide and starch through which it passes may be capable of roasting a potato, cooking an egg or a piece of meat. A galvanic current which would produce only an insignificant amount of heat, if passed through the same solution, would decompose the iodide and discolor the starch. Again, the galvanic currents in which the potential is suddenly changed, and alternating currents of all kinds except the high frequencies, have for a prominent characteristic the ability to cause muscular contraction. The high-frequency currents, on the other hand, probably because the vibrations are above the nerve register, produce no muscular contractions even with the strongest currents.

There are several methods of applying the high-frequency currents for therapeutic purposes, according to the particular action desired. In general, the results obtained may be divided into those due to constitutional effect and those where the effect is local. For constitutional effects autocondensation and autoconduction are the principal methods used.

Autocondensation.—In this method the d'Arsonval current is used, and the patient is placed upon a special chair or couch, the cushions or supporting surfaces of which have a lining of metal, over which is placed a heavy, insulating layer. One of the terminals supplying the d'Arsonval current is connected with the metal lining of the chair or couch, and the other with the body of the patient, usually the hands. A meter is connected in series with the patient, and with the more powerful currents will register 1000 or 2000 milliampères. The patient feels little or no sensation, although vacuum tubes placed near him will be strongly illumined.

For *autoconduction* no contact of any kind is made with the patient, but he sits within the spirals of a large coil of wire, the terminals of which are connected with those supplying the d'Arsonval current; the effect is similar to that of autocondensation. These two forms of treatment are most largely applied to reduce **high blood-pressure** and for **deficient metabolism.** After applications of from ten to thirty minutes there is a distinct rise in temperature, excretions are stimulated, and the blood-pressure notably reduced in cases of hypertension. The static currents are unsuitable for this form of application, as the ampèrage is insufficient for any decided effect.

Diathermy, or *thermopenetration*, signifies the thermic effect of the d'Arsonval current, which is very considerable under certain conditions. This also requires heavy ampèrage, for which the static current is inadequate. Two metal electrodes are applied to the part of the body that requires treatment, and the current is increased until the desired result is obtained. There is little danger of doing harm, as the toleration of the patient is reached before any burn is produced. The effect appears to be purely thermic, and is applicable to conditions where heat is indicated. By this method the penetrating effects of heat can be produced more effectively than by any other method.

High-frequency currents may be applied locally by means of various electrodes, of which the glass vacuum tubes have the widest range of use. By means of these either the d'Arsonval or the Oudin current may be applied, giving both constitutional and local effect. The constitutional effect is similar but less than that produced by autocondensation, and the local effect varies with the type and strength of current used, and with the manner of application. With the electrode in contact with the skin the only sensation caused is that of warmth, the d'Arsonval current being the more penetrating. If the vacuum electrode is held at a distance from the surface, a multitude of fine sparks are discharged into the skin, producing a sharp sensation and a marked hyperemia of the cutaneous surface.

From metal electrodes the sparks are sharper and have a cauterizing effect. Electrodes connected with the Oudin current held at some distance from the surface cease to discharge sparks, which are replaced by a spray-like discharge called the *effluve*. The sensation produced is very mild and the effect superficial and mildly anesthetic.

Applications of the high-frequency currents, both the d'Arsonval and the Oudin, are of great value in the treatment of painful conditions, such as **neuralgia, neuritis, myalgia,** and **arthritis**; and also for many cutaneous affections, as **eczema, ulcerations, lupus,** etc.

Fulguration.—The cauterizing effect of the high-frequency spark from pointed metal electrodes has been utilized for the destruction of small neoplasms, angiomata, etc., and has considerable latitude of application. With the d'Arsonval current bipolar application may be made, placing a large neutral electrode opposite the area to be treated. Unipolar applications are less penetrating. The pointed electrode is held at or near the surface to be treated, the vitality of which may be rapidly destroyed. If the bipolar method is used deep cauterizing effect can be produced with almost the same accuracy as with a knife. The destroyed tissue ultimately sloughs and the wound heals by granulation. The effect is not selective, but destroys healthy as well as abnormal tissue. With the Oudin current long, heavy sparks may be used by bipolar application, giving a more superficial cauterizing effect.

The term *desiccation* has been given by Clark to his method of employing the high-frequency current from high-powered static machines for the destruction of tissue. With a carefully adjusted current from the resonator, by means of short, rapid sparks from a pointed electrode, the effect is sufficient heat to devitalize but not to burn the tissues.

Sinusoidal Currents.—In some alternating currents the transitions from one phase or polarity to another is sharp or abrupt, rendering the effect biting and unpleasant when applied therapeutically. An alternating current in which the changes in polarity are gradual has been termed the sinusoidal current because the graphic curve of the wave is similar to the geometric sine curve. In therapeutics sinusoidal currents are employed having a potential with a maximum of about 110 volts, and are usually generated by special generators. The commercial alternating current can be utilized by means of transformers and controllers, but is not entirely suitable for this purpose. The value of this current in therapeutics depends upon its faculty of producing a maximum of muscular contraction with a minimum of discomfort to the patient, in this respect resembling the static-wave current. The sinusoidal will often cause contractions in muscles where faradism fails on account of a partial reaction of degeneration associated with disease of the motor nerves. It may be found useful, therefore, in **muscular paresis** or **paralysis.**

Magnetic Wave Currents.—The magnetic field of electromagnets, actuated by an alternating current, has been utilized therapeutically, placing the patient between two magnets of opposite polarity. Although no sensation is felt by the patient, this treatment is said to have a general effect of **deficient metabolism** and reducing **high blood-pressure.**

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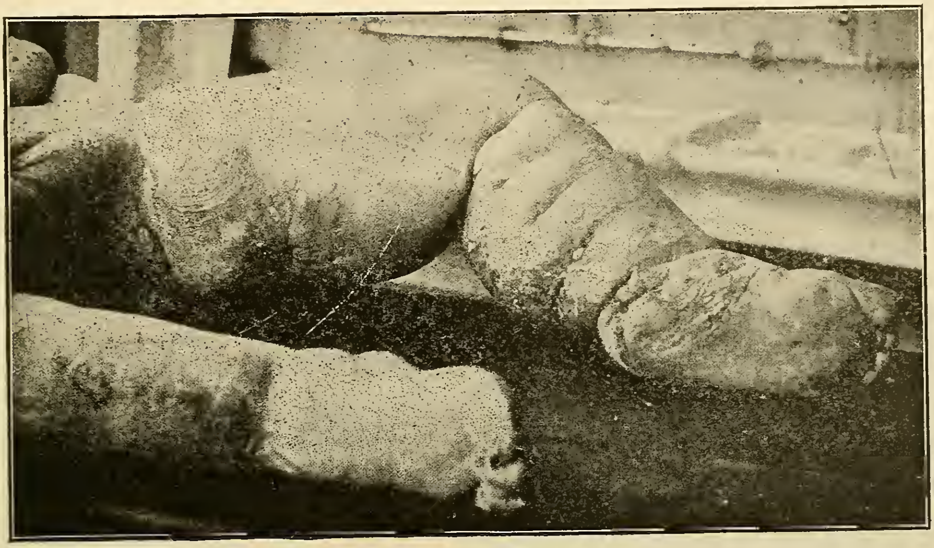
ELEPHANTIASIS.—Elephantiasis arabum; pachyderma; elephant leg; Barbadoes leg.

DEFINITION.— Elephantiasis is a chronic hypertrophic disease of the skin and underlying tissue due to obstruction of the lymphatic channels by parasites or other causes, and resulting in enormous enlargement and thickening of the part, with or without papillary overgrowth.

SYMPTOMS. — The term "elephantiasis" was used by the Greeks to designate the malady now called leprosy. Elephantiasis græcorum is, therefore, to be distinguished from elephantiasis arabum. The most frequent seats of elephantiasis are the lower extremities, although the penis, scrotum, labia, and clitoris may be affected, and more rarely the arms, lips, tongue, or ears.



Elephantiasis. (*W. K. Hunter.*)
(Glasgow Medical Journal.)

There are two forms of the disease, the one, *endemic,* is parasitic in origin and indigenous to the tropics; the other, *sporadic,* is due to inflammatory obstruction of the lymphatic or blood-vessels and observed in various countries. There is also a congenital form of elephantiasis, which is extremely uncommon. The tropical form is rare in the United States; we will, therefore, restrict our description to the ordinary variety.

The disease usually begins as an erysipelatoid inflammation, accompanied by fever, redness, swelling, heat, and pain. The condition may represent a dermatocellulitis, a lymphangitis, or a phlebitis. After some days the inflammatory phenomena subside, but the affected part is observed to be larger than before. Similar attacks may recur from time to time, at intervals of weeks or months, the affected part increasing in size after each attack. Finally, a state of chronic hypertrophy is reached, the skin and subcutaneous tissue are enormously thickened, and the member greatly increased in diameter.

The skin is glossy and tense and the deeper structures resistant and dense, as a result of which digital pressure produces but slight indentation or none at all. The surface may be pigmented, exhibit warty excrescences or thickly studded papillomatous vegetations. These consist often of lymphatic varicosities, the elevations occasionally discharging a chylous or milky fluid. Between the papillary overgrowths, fissures of varying depths are observed.

Maceration of the epidermis and the collection of decomposing sweat, sebum, and effete products give rise to an offensive odor, particularly where habits of cleanliness are not observed. There is, as a rule, no pain, although during the acute inflammatory exacerbations it may be severe. The enormous weight of the hypertrophied part may make locomotion difficult or even impossible. The course of the affection is chronic.

ETIOLOGY.—The disease is most common in tropical countries, particularly Africa, India, China, Japan, West Indies, etc., where it occurs chiefly in those subject to bad hygiene and poor food. Damp, malarial districts are said to produce the largest number of cases. This is explicable upon the theory now proposed, that the mosquito is the intermediate host of the filariæ. The tropical form is due to inflammation and obstruction of the lymphatic vessels by the *Filaria sanguinis hominis*. The parasites are most likely to be found in the blood at night; blood examined in the morning usually fails to show the presence of the filariæ. They appear as transparent, serpentine, wriggling, wormlike creatures inclosed in a sac or sheath.

Sporadic cases may be due to inflammatory obstruction of lymphatic and perhaps other vessels, following repeated attacks of erysipelas, and as a result of cellulitis, infection from ulcers, syphilis, pressure of scars or tumors, etc.

Case in which a verrucose tuberculous condition of the sole of a foot, in a patient "scrofulous" since childhood, was followed by lymphangitis in the lower portion of the leg and a progressive sclerosing inflammation with edema. The ultimate result was a condition of elephantiasis, which in this case was manifestly of tuberculous origin. Gongerot (Revue de chir., July, 1912).

PATHOLOGY.—There is a hyperplasia, participated in by the subcutaneous tissue and all of the layers of the skin. The chief change is in the subcutaneous tissue, which is enormously hypertrophied and traversed by irregular bundles of connective tissue. Where the surface of the skin is warty, the papillæ are greatly elongated. Both blood-vessels and lymphatics are enormously distended, the latter leading to dilated lymph-spaces. The neighboring lymphatic glands are enlarged. In advanced cases the muscles undergo fatty degeneration and the bones become enlarged.

The essential characteristics of the acquired form of the disease are lymphangiectasis, hyperplasia of connective tissue, and chronic edema, and these conditions may frequently be attributed to the interaction of stasis and inflammation, stases always occurring early, and persisting. Inflammation may precede or follow stasis, or may be absent at any stage of the disease, and may be acute or chronic and generally may be traced to bacterial infection. Chronic stasis or inflammation may predispose to elephantiasis, but the disease does not always result even when they occur together. Filaria is an important factor in the production of endemic elephantiasis of some countries, but is not essential to the occurrence of the endemic variety. G. C. Shattuck (Boston Med. and Surg. Jour., vol. clxiii, No. 19, 1911).

DIAGNOSIS.—The history of recurrent erysipelatous inflammation, with slowly progressing hypertrophy, is commonly noted in the sporadic form of elephantiasis. In advanced cases, particularly of the tropical variety, the appearances are unmistakable, the enormous enlargement of the affected member being absolutely characteristic.

> Case of tuberculous elephantiasis described and 7 cases on record. The diagnosis from syphilitic or filarial elephantiasis is made by the ophthalmic and Wassermann reactions, microscopic examination of a piece of tissue cut from the growth, and the presence of other symptoms of tuberculosis: fever, loss of weight, enlargement of inguinal glands, tuberculous foci in the lungs, etc. Daniel (Monats. f. Geburtshülfe u. Gynäk., Jan., 1913).

PROGNOSIS.—In the beginning the process may at times be arrested. When the growth is far advanced, treatment accomplishes but little, though some recent surgical measures (see TREATMENT) may afford some hope. Very severe cases may terminate fatally.

TREATMENT. — The erysipelatous attacks are to be treated by **rest, hot** or **cold applications, elevation of** the **affected member,** and the internal administration of **salines** and **quinine.** Quinine is especially useful in elephantiasis contracted in malarial regions.

> Dr. Dubriel de Broglie, of the French colonial medical service, recommended the internal use of 30 drops of the **tincture of the chloride of iron** three times daily, in combination with bandaging of the affected limbs and complete rest in bed. The writer determined to make the experiment of administering the tinctura ferri chloridi without bandaging and permitting the patient to follow his usual mode of life. In every case so treated, the patient has shown decrease in the size of the affected part within a few weeks, and the effect on the fever is apparent even sooner. He therefore concludes, as a result of these experiments, that tinctura ferri chloridi has a marked effect on the elephantoid process, decreasing the size of the affected parts and restoring function to an even greater degree. Its most marked effect, however, is on the attacks of *elephantoid fever,* these attacks being markedly lessened in severity, the interval between attacks being greatly lengthened, and in several of the cases the attacks have apparently ceased. In one of prolonged elephantoid fever with very marked chyluria of three weeks' duration, the chyluria disappeared entirely within sixty hours under the administration of tinctura ferri chloridi alone. So far as can be judged from the number of cases treated, elephantiasis appears to be arrested by this treatment if continued for six to twelve months, and if some method can be devised in conjunction therewith to dispose of the elephantoid tissue already formed, the author believes that a cure may be looked for. P. S. Rossiter (United States Naval Med. Bull., July, 1909).

Good food and **hygiene, tonics,** and **change of climate** are important features in endemic cases. Elastic compression by means of a well-applied **rubber bandage** is the most efficient therapeutic measure. **Green soap** and the **mercurial ointments** may be rubbed into the skin. The long-continued use of the **galvanic current** has occasionally given good results.

In advanced elephantiasis of the leg one may resort to **stretching** or **partial exsection of the sciatic nerve,** or digital or **instrumental compression,** or even **ligation of the femoral artery.**

Elephantiasis of the scrotum is best treated by **amputation.** Various surgical measures have been introduced in recent years.

> Case in which so great and striking improvement followed **angeioplasty** as to justify the hope that a cure had been found. In this operation a number of stout silk threads running the whole length of the limb are introduced into the subcutaneous tissue of the swollen

part. The threads are completely and permanently buried. Their capillary action enables them to replace the trunk lymphatics and to transfer the excess of fluid from the area of lymphatic edema to regions where the lymphatic circulation is normal, and where consequently the excess of fluid is absorbed and carried off into the general circulation. Handley (Lancet, Jan. 2, 1909).

The cases of elephantiasis witnessed by the writer were due usually to repeated attacks of erysipelas, in which phlebitis and lymphangitis lead to an inflammatory obstruction of the lymph-vessels or from the obstruction of the lymph due to the removal of lymph-nodes by operation. In most of them a transitory edema developed, but in some the lymph-stasis became permanent and was accompanied by thickening of the subcutaneous tissue. In a troublesome case, after a trial of ten days' elevation of the right leg without much success, the writer made an **incision** on the outer side of the thigh in its whole length, dividing the fascia lata and exposing the bone behind the posterior edge of the vastus externus muscle. After separating the periosteum from the bone, three openings were made into the medulla, in the upper, middle, and lower thirds of the femur. Narrow **strips of fascia lata** were then **excised,** which were introduced into the bone openings, with the hope that along them a collateral circulation of the lymph would develop. The facial wound was then closed by a suture and many small openings made in the fascia with scissors to favor the escape of the lymph. The skin wound was closed and a collodion dressing applied. The patient left the hospital a few weeks with the wound healed. A year later he reported for examination, when the wound was still healed. Three years after operation examination showed the following result: While before the operation he was compelled from time to time to stop work for three hours and lie down, immediately after the operation he began to improve, and at the present time he can work all day without difficulty. The case was virtually cured. Lanz (Zentralbl. f. Chir., Bd. xxxviii, Nu. 3, 1911).

Case in which the writer restored the patient to active life by a combination and modification of Lanz and Oppel's methods for diverting the course of the lymph by **anastomosis between** the **superficial and deep lymphatics.** Diamond-shaped patches of skin, 15 or 11 cm. across, were cut out of the thigh and calf. The subcutaneous tissue and aponeurosis were cut across on the short diameter of the diamond and then cut along one side line down to the muscle. This produced two triangular flaps; each was turned over and pushed into the space below between the layers of the muscle separated for the purpose with a blunt instrument. The flaps were held with a few catgut stitches in the muscles and periosteum. The skin was drawn together and sutured along the long diameter of the diamond, thus exerting compression on the lymphatics below. Rosanow (Archiv f. klin. Chir., Bd. xcix, Nu. 3, 1912).

The writer performed **Handley's operation** (*vide supra*) in 2 cases of elephantiasis of the lower extremities. The results were excellent. Great care is necessary to bring about and maintain perfect asepsis as well as prolonged absolute rest. The best results were obtained with the patient whose leg was immobilized for two and a half months. Bilim-Kolosovsky (Roussky Vratch, April 28, 1912).

The writer tried the methods of Lanz and Handley and found them useless, because there was in all his cases a very thick fascia which prevented the lymph communication between the muscles and the subcutaneous tissue. He therefore attempted to restore this continuity by removal of large areas of fascia. This was done by making long and broad **incisions** followed by the **removal of** an area of **fascia** corresponding. In 6 cases the operation was attended by excellent results and increased usefulness of limbs. E. Kondoleon (Zentralbl. für Chir., July 27, 1912).

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Philadelphia.

EMBOLISM.— DEFINITION. — Embolism is the obstruction of some portion of the vascular system and arrest of the circulation by a plug conveyed in the blood-current. The obstructing body, which may consist of organic or inorganic material, is termed an embolus. Thrombosis and embolism are often associated, a thrombus when dislodged from its position becoming an embolus, and the latter, by deposit of coagulum, growing into a thrombus. Embolism affects arteries and capillaries and, also, the portal vein on account of the anatomical arrangement of that vessel. The exceptional involvement by retrogression of other veins and of the lymphatics will be subsequently considered.

SYMPTOMS. — In general terms these relate to the resulting anemia, necrosis, sloughing, sepsis, and abolishment of function. Mild degrees of embolism occasion little or no constitutional disturbance, while the local manifestations may be so slight as to render the ordinary methods of physical examination useless or inconclusive. The symptoms are manifold, however, in the severer forms of obstruction, and vary according to the character of the embolism and of the vessel or structure involved.

> Cases of fatal postoperative embolism since the opening of the Mayos' clinic, September 30, 1889. The total number of deaths in the hospital for the period under consideration, from all causes, was 864, of which the fatalities from embolism were approximately 5 per cent. The mortality from embolism, based on 63,573 operations, is 0.07 per cent., or 1 death in every 1352 operations. Twenty-six of the patients were males and 21 females, the youngest being 25 years of age and the oldest 72. Forty-one of the patients had been from two to thirty-five years subject to some form of severe chronic debilitating disease. Nineteen of the fatalities occurred within the first week after operation, 21 more within the second week, 4 in the third week, and 1 each on the twenty-sixth, the thirtieth, and the sixty-fourth days, respectively. In 36 of the cases the embolism was pulmonary, in 10 cerebral, and in 1 coronary. In 28 of the 41 cases posted, the originating thrombus was found in the field of operation or the femoral vein.
>
> From a study of his cases and of the literature, the writer calls attention to the following general considerations: 1. Following operations, particularly on the blood-vessels, alimentary canal, and genitourinary organs, from 1 to 2 per cent. of all cases give more or less distinct clinical evidence of emboli, above 70 per cent. of which are in the lungs. 2. About 10 per cent. of postoperative emboli which give clinical symptoms of diagnostic significance cause sudden death. 3. The source of the emboli can be definitely determined by autopsy as venous thrombosis in about 80 per cent. of the cases, as cardiac thrombosis in 10 per cent., while 10 per cent. are scattering or indeterminable. 4. The most important factors are the injury of the vascular walls, slowing and stagnation of the blood-stream, the disintegration of the corpuscles of the blood from toxic substances and bacteremia. 5. In consideration of the above-mentioned factors the following precautionary measures suggest themselves: 1, the reduction of vascular traumatism to a minimum; 2, the encouragement of very early free movement on the part of the patient; 3, the preoperative administration of drugs to increase the coagulability of the blood; and, 4, measures looking toward the reduction of bacteremia. L. B. Wilson (N. Y. Med. Jour., from Annals of Surg., Dec., 1912).

One of the most common forms of embolism is produced by thrombi originating in the endocardium, in atheromatous patches of the aorta, and in the large veins of the pelvis and lower extremities. A calcareous or vegetative fragment from a diseased valve or intima in aortic obstruction or ulcerative endocarditis is a frequent source.

Equally frequent causes of embolism are fat particles from fractures of the bones, with laceration of the marrow; from contusions of the adipose tissue, and from injury to various fat-containing organs or structures of the body. Other sources of embolism are tissue fragments, pieces of a tumor projecting into a vessel, pigment particles in disorganization of the blood by malaria, and small hyaline masses occurring in burns and certain kinds of toxemia. Emboli may consist, also, of giant cells derived from bone-marrow and the chorionic villi, parenchymatous cells from the liver, spleen, myocardium, and other structures, or tumor-cells. Lastly, embolism may result from bacteria, scolices of echinococcus or other parasites, and from foreign bodies, such as air and dust. It has been claimed that embolism occurs more frequently in females than in males, and that of all the valvular lesions giving rise to it mitral stenosis is the most common.

In a case witnessed by the writer, the patient suddenly became dizzy and vomited and her left arm fell helpless to her side. Three days later, with the same symptoms, she suddenly lost power of motion in her left leg and foot. Marked trophic changes soon took place in the affected parts; they were colder than the corresponding portions on the other side of the body; some movement was possible in both extremities, but there were no other signs of paralysis here or elsewhere. Pulsation was absent from the arteries of the left forearm below the brachial artery and in the palpable arteries of the left lower extremity. Four days after she was first seen, she died very suddenly. Autopsy showed the presence of a marked mitral stenosis and of a large ante-mortem clot in the left auricle. Obstruction of the vessels in the extremities was due to emboli, one in the brachial, the other in the lower half of the femoral. Alderson (Brit. Med. Jour., Oct. 26, 1912).

The location and distribution of embolism depend chiefly upon the source. Emboli in the general venous circulation usually pass through the right heart and lodge in some branch of the pulmonary artery. Those in the portal circulation are either arrested in the liver or borne to the heart and lungs, while those originating in the left heart enter the general arterial circulation and may be widely distributed to the different organs of the body and the peripheral vessels, but are most frequently found in the spleen, kidneys, and brain. As a rule, emboli follow the blood-current and finally lodge at the bifurcation of a vessel or at a point where the size of the tube renders further progress impossible, although a soft embolus impacted against a bifurcation may split into fragments, which enter the smaller branches of the artery.

A circular letter to 25 of the most prominent surgeons of Boston and vicinity brought out that thrombosis and embolism are more common after operations in the pelvis than after operations in any other part of the body, and also that many cases of pleurisy, pneumonia and pulmonary abscess following operation are probably due to emboli. Large emboli almost always cause speedy death by syncope or asphyxia; very small emboli usually run a favorable course. Any sudden increase in pulse rate during convalescence, temperature remaining about normal, should suggest the possibility of thrombosis. Dearborn (Annals of Gynec. and Ped., Nov., 1904).

In surgery, embolism, aseptic or septic, is the commonest cause of sudden death, and the general distribution is as follows: (1) pulmonary, 70 per cent.; (2) renal, 12 per cent.; (3) splenic, 8 per cent.; (4) hepatic, 5 per cent.; (5) cerebral, 4 per cent.; (6) pleura, peritoneum and joints, 1 per cent. The risk of sudden postoperative death from embolism can be decreased by insisting on from 48 to 72 hours' anatomical and physiological rest before operation, and by taking care that the intestinal and urinary systems are thoroughly cleared. B. Robinson (Med. Rec., Jan. 14, 1905).

To the general rule above stated there are two exceptions: paradoxic and retrograde embolism.

The term *parodoxic embolism* is applied to the entrance into the general circulation of venous emboli through a patent foramen ovale or ductus arteriosus, or a perforated ventricular septum. Emboli in the lungs may be broken into smaller fragments—as often occurs in fat embolism—and, penetrating the pulmonary capillaries, enter the general circulation.

Another variety has been termed *retrograde embolism*. In whooping-cough, emphysema, and other affections of the respiratory organs in which the intrathoracic pressure is increased, with positive instead of negative pressure in the large intrathoracic veins, emboli in the form of tumor fragments, cellular bodies, microbes, or other material may be carried in a direction opposite to that of the normal blood-current. From the inferior vena cava, for instance, the plug enters the hepatic vein and lodges in the liver, while the peripheral veins of the body may be occluded by emboli coursing backward from the right heart. In such instances there is either a reversed current from obstruction at the right auricle or successive cardiac impulses, sending the impacting body in a backward direction. In this connection reference can be made to an apparently retrograde embolism in the lymph-vessels, which is stated to be due to occlusion and dilatation of the vessels, with incompetent valves, and a consequent backward flow. Another explanation is that tumor-cells have the power of moving in this direction, the result being, for instance, malignant disease of the lymph-glands from tumors situated on the distal side.

The writer's experiments warranted the following conclusions: Thrombosis of veins of the omentum is readily produced by mechanical, thermal, and bacterial agencies. From thrombosed omental veins emboli may frequently separate, probably owing to the periodical vasodilatation and contraction associated with the ingestion of food. Emboli from veins in the omentum may, under certain circumstances, be carried up gastric veins and become impacted in the venous plexus of the submucous coat of the stomach, and determine a gastric ulcer. Beyond this it is impossible to go at present, but these experimental results prompt certain suggestions in regard to the etiology of gastric and duodenal ulcers in the human subject which can only be decided by prolonged and extensive clinical investigation. These suggestions are: That the hematemesis sometimes met with in cases of acute appendicitis is due to an acute gastric ulcer resulting from blockage of a gastric vein by a septic embolus from a thrombosed omental vein. That on similar lines the omental vessels may form the connecting link in the association of chronic gastric or duodenal ulcer with an inflammatory process in the lower abdomen. One might even go further and suggest that the relatively greater frequency of duodenal ulcer in the male is directly associated with his greater liability to appendicular trouble and consequent involvement of the right border of the omentum, while the relatively greater frequency of ulceration of the body of the stomach in the female is associated with her exposure to pelvic inflammatory trouble which may occur on either side and may involve any portion of the omentum. The ulcers which were produced experimentally were of the acute type, and they tended to heal up readily, for the animals used were healthy and lacked the very important factors which appear to determine the chronicity of gastric ulcers in the human subject, namely, the general irritability of the gastric mucosa and the altered secretory function of the gastric glands. The occurrence of embolism of veins in the pancreas, followed by hemorrhages into the pancreatic tissue, after the injection of artificial emboli into omental veins, suggests the possibility of portal embolism playing a part in the etiology of some cases of acute pancreatitis. D. P. D. Wilkie (Edinburgh med. Jour., May, 1911).

Emboli may also occur in *special locations.* Embolism of the aorta, of the superior mesenteric artery, and of the spinal cord is uncommon, and, in many instances, does not admit of easy diagnosis. Emboli may lodge in the small intestinal arteries. More frequently, the lungs and brain are involved. The kidney is said to furnish 66 to 75 per cent. of cases, and the spleen is next in frequency. In typhoid fever 6 per cent. of the fatalities are ascribed to pulmonary infarcts.

Postoperative pulmonary embolism was observed in 57 out of a total of 6871 operations in von Eiselsberg's service at Vienna since 1901. In 23 cases the fatal embolism did not become infected; in 20 cases there were infarcts, and in 14 there were embolic-suppurative processes. There were also noted pulmonary complications in 263 cases, that is, 3.8 per cent., but of embolic nature in only 0.8 per cent. A laparotomy has been done in 24 and herniotomy in 12 of the embolic cases. In the 23 fatal embolic cases death occurred in a few minutes from the first symptoms of the embolism in 5 cases, while in 9 several hours elapsed before the fatal termination. In 3 the symptoms of embolism were observed immediately after the operation. Ranzi (Archiv f. klin. Chir., Bd. lxxxvii, Nu. 2, 1908).

The writer was able to find some primary infectious focus in every case of fatal pulmonary embolism from primary venous thrombosis. In some cases the walls of the vein are inflamed, but in others infection of the blood is responsible for the intravascular coagulation. Kretz (Med. Klinik, Oct. 10, 1909).

Since 1899 there occurred in St. Luke's Hospital 15 cases of sudden death following operation which have been attributed to pulmonary embolism. Such autopsies as have been performed have verified the condition. Special attention is called to three main factors: The age of the patients—young individuals are more or less exempt, and if affected may perhaps recover presumably on account of the yielding elasticity of their vessels, which may allow the blood to push its way beside a clot. The age from 40 to 60 being most afflicted, we are probably dealing with conditions of vascular changes over which the operator has little or no control. Practically all those cases of embolism follow interventions below the diaphragm and even lower. Gibson (Med. Record, Jan. 9, 1909).

The mortality statistics of embolism of peripheral origin show a high death rate. Lenormant collected 233 cases where it had followed surgical operations, and found that 106 (45.5 per cent.) ended fatally, but such statistics undoubtedly exaggerate the mortality, since they contain a disproportionate number of serious cases. In those of cardiac origin, embolism is often a terminal event and usually indicates the beginning of the end. According to Romberg, 36 of 43 patients with heart disease in the Leipzig Clinic, in whom a positive diagnosis of pulmonary embolism was made, died. Three striking instances witnessed by the writer raised a question as to the frequency with which they are overlooked, because their possibility is not considered in making a differential diagnosis. Some cases must necessarily escape detection because they cause no symptoms; others because they are terminal events occurring when the patient is already in a serious condition, if not *in extremis,* and the symptoms are confounded with those of the primary disease. The most characteristic symptoms are dyspnea, cough with bloody expectoration and pain, but the suddenness of its onset alone gives the first distinctive significance. The other two are so infrequent that their absence is of little importance. The discovery of physical signs of consolidation in the lungs may be of assistance in diagnosis, though a large infarction may lead to error by suggesting a pneumonic process. It may resemble one of the following conditions: cardiac asthma, acute dilatation of the heart, angina pectoris, pneumonia and pleurisy, phthisis, bronchitis and neuralgia. Sears (Boston Med. and Surg. Jour., April 28, 1910).

A study of 25 cases of fatal pulmonary embolism that occurred in the writer's service in the last eight years showed one common factor in all, viz., that organs containing infectious germs were opened in the course of the operation. Further study of the technique has convinced him that some of these germs must have found their way into gaping veins and that the latter were responsible for the development of thrombosis and subsequent embolism. J. Veit (Zentralbl. f. Gynäk., Jan. 1, 1910).

Embolic infarcts may occur at any place in the lung, irrespective of the primary site of the embolus. The part most commonly involved is the lower lobe. Reye (Zentralbl. f. allg. Pathol. u. Path. Anat., Dec. 15, 1912).

Experiments have been reported which give some ground for the belief that cerebral embolism and chorea may be related as cause and effect, but corroborative clinical evidence is wanting.

The writer witnessed 2 cases of cerebral embolism neither of which presented the characteristic symptoms. In the first case the man drank a cup of coffee, tried to stand up, and then learned that his left arm and leg were paralyzed. He did not lose consciousness at all and the paralysis soon passed away. For two days he ate, drank, and felt well. He then became unconscious and remained so until his death eleven days later. Autopsy revealed an embolism of the artery of the Sylvian fossa on the right side, with some softening of the brain. In the second case, a boy, 15 years old, convalescent from diphtheria, suddenly began to vomit frequently, became very pale, had facial spasms, finally paresis of the left side of the face, uttered from time to time a cry like the hydrocephalic cry of children with meningitis, and grated his teeth. At times he was apathetic, at other times restless. On the morning of the day of his death there was noted a slight facial paresis on the left side, vomiting, great thirst, and no paralysis of the limbs; he ate, drank, and slept well; the pupils were alike and reacted promptly. Lumbar puncture revealed nothing pathological. That evening he died and the autopsy revealed an embolus of the right artery of the Sylvian fossa, dense, dry, and extending into the finer branches of the artery. The lesion therefore in both cases was the same, but the clinical courses differed both from each other and from that which usually accompanies such a lesion. Hippel (Med. Klinik, Jan. 22, 1911).

As to the *results of embolism,* sudden death is apt to follow the occlusion of the coronary artery or one of the large vessels in the lungs or medulla; but a fatal termination may be delayed in partial obstruction leading to thrombosis. The effects of embolism depend, therefore, upon the amount of obstruction, the character of the occluded vessels, and the particular area involved. When the anastomosis of the vessels is free, the increase of blood-pressure and the dilatation of the relieving vessels on the proximate side of the plug compensate for the transient anemia on the distal side. Thrombosis occurs before and behind the obstruction, extends in both directions to the nearest vessels, becomes organized, and reduces the involved vessel to a solid cord. Connective-tissue proliferation takes place in the vessel. The same compensatory changes occur in capillary embolism, and in both instances the damage inflicted is trivial, consisting only of the loss of a portion of the circulation. With multiple embolism, however, the results may be of the most serious character.

> Large emboli following abdominal section usually cause speedy death by syncope or asphyxia, but small emboli usually run a favorable course. Thrombosis may result, (1) after a prolonged or severe operation; (2) as the result of sepsis in the wound; (3) without either of the above conditions. Pulmonary embolism most frequently result from thrombi in the venous system. The latter are most frequent in the leg, as in fractures and protracted fever. Emboli resulting from thrombosis of veins after pelvic and abdominal operations come next in frequency. There is practically no treatment for the severe cases. A careful study of the blood before operation, avoidance of profuse hemorrhage during the operation, and **saline infusions** after the operation may diminish the frequency of such cases. Wilmer Krusen (Amer. Jour. of Obstet., April, 1906).

> In the differential diagnosis of embolism, where trauma precedes this condition, there are three things to consider —shock usually occurs within three hours, fat embolism three days, pulmonary embolism three weeks. Seventy per cent. of all emboli probably enter the pulmonary artery. As these bodies most usually originate in a vein, they enter the right side of the heart; consequently the pulmonary artery is a favorable site for their migration. The clinical history of many cases of embolism would indicate that this condition frequently occurs simultaneously with, or following some bodily movements, or excitement, as walking, laughing, or other muscular movements, which seem to aid in liberating these bodies; and when once detached evidently they soon reach their final destination. Embolism may terminate in one of three ways—in instant death, in delayed death, or in recovery. Study (Med. Record, March 16, 1907).

Infarction results from the occlusion of end-arteries, such as are found in the lungs, brain, spleen, kidney, mesentery, retina, and portions of the heart. Anemia with necrosis may occur, or else a transient anemia followed by a backward flow of venous blood, causing engorgement or hemorrhagic infarction. The tissue involved, or infarct, is denser than the surrounding area, wedge-shaped, red, and pulpy, with the apex pointing to the embolus. At other times the area affected is of a grayish color, the white infarct. The shape of an infarction is irregular when several vessels are blocked. These results are not uniform, however, in the case of structures supplied by end-arteries. Exceptions are noted when the surrounding blood-supply is free, as, for instance, near the root of the lung, whereas a striking example of the red infarct is found in the periphery of that organ. In the spleen, infarction is the rule, and coagulation necrosis is apt to occur in the kidney, although the affected tissue is wedge-shaped. In the brain and retina, necrosis with softening ensues. In the liver the blood-supply from the hepatic artery suffices for a limited secretion of bile, even with obstruction of the entire portal vein. When the superior mesenteric atrery is involved, infarction is the rule, while sloughing and hemorrhage occur. The ultimate effect of embolism after anemia and necrosis is the loss of tissue by sloughing, cicatrization, and absorption.

Septic emboli, in addition to their mechanical effects, are the carriers of infection, and when disintegrated become the distributors of micro-organisms from their point of lodgment to the system at large. Typical examples occur in septic endocarditis or in infectious embolism of the lung. Secondary infection of bland infarcts may occur. Thus the so-called metastatic abscesses have their origin, and septicemia is apt to follow. Multiple tumor growth may be caused by cells brought from a tumor of like character located at a distance, while microbic action at the seat of occlusion may so affect the vessel wall as to produce what has been termed embolic or mycotic aneurism.

Fat embolism, which probably occurs to a greater or less extent in all cases of bone-crushing or contusion of adipose tissue, may have no pathological or clinical significance. In mild forms the fat particles are absorbed in the pulmonary capillaries, or pass through them in subdivisions, to be absorbed in the circulation or in the spleen, liver, kidney, or other organs. When the amount of fat is considerable and widely distributed, the most serious consequences may follow. In such cases there are dyspnea, quickened respiration and pulse, and, in a word, the usual symptoms of respiratory obstruction, which appear usually in from thirty-six to seventy-two hours. In fatal cases death supervenes upon cyanosis, delirium, and coma, with profound asthenia. The temperature, at first subnormal, may remain so or be elevated. The presence of fat globules in the urine is noteworthy and of diagnostic importance. Fat embolism is to be differentiated from shock, acute pulmonary and renal congestion, acute septicemia, and ether anesthesia. The prognosis is favorable after twenty-four hours.

Fat embolism is due to the crushing of the bone-tissue forcing fat into the veins in the bones. The writer's clinical experience indicates the importance of refraining from crushing the bone in operations. Bergemann (Berl. klin. Woch., June 13, 1910).

Cutting injuries of bones are liable to lead to fat embolism, the veins in the bones taking up the particles of fat. Mere concussion of the bone was sufficient, however, in some cases to induce fat embolism by the lymphatic route, the lymphatics taking up the fat particles and thus passing them along into the circulation. In *lymphatic fat embolism* prompt drainage of the thoracic duct warded off danger when the operation was done at the first signs of fat embolism. Fritzsche (Deut. Zeit. f. Chir., Nov., 1910).

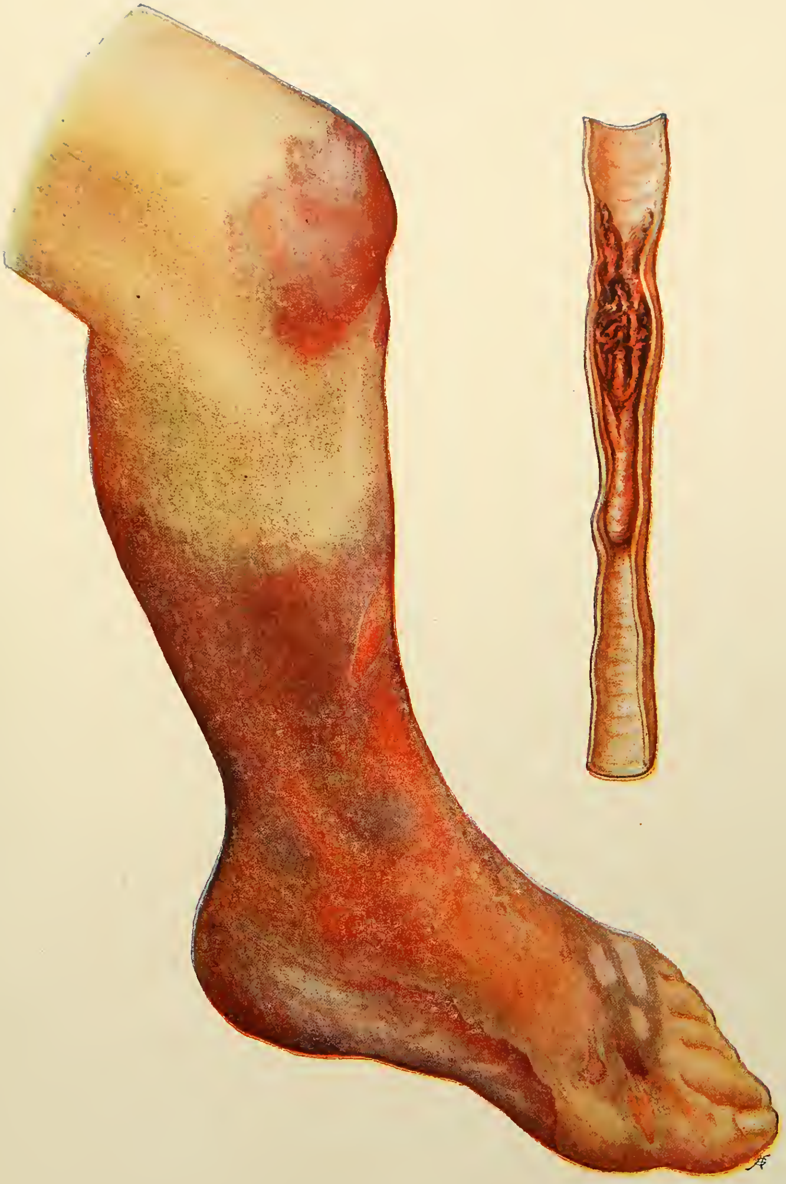
Cases of fat embolism are reported only when severe and when they have a fatal outcome. Most of the cases follow orthopedic operations and fractures. The view is gradually gaining ground, however, that fat embolism is a much more frequent occurrence than formerly was supposed possible. Leading authorities have long insisted on the difficulty of diagnosing it, but in 3 cases in the writer's practice in the last six months there were punctate cutaneous hemorrhages, and he thinks that this sign may reveal the fat embolism in many cases which otherwise would escape detection. He has been unable to find similar cases on record. Benestad (Norsk Magazin f. Laegevidenskoben, March, 1911).

Case of fat embolism. The patient, a girl, aged 19, had typhoid fever at the age of 10 and since then the distal end of the femur had been the seat of a chronic inflammation with a discharging sinus. In the fall of 1910 it was operated on and the sinus healed and gave no further trouble until March, 1911. On her way to Rochester, March 12th, she stopped off at Canby and consulted the author on account of difficulty in breathing, and a few days later the recurring paroxysms of dyspnea prevented sleep; the pulse range was from 93 to 140. She was cyanotic and the heart action weak; there was retention of urine and vomiting. March 20th she became comatose and pulseless for forty minutes after a terrible struggle for breath. The next day fat globules were abundant in the urine. The patient was improved somewhat, but became critical again on the following day. Later there was slow improvement but mild attacks of dyspnea. She went west hoping to be benefited from a change of climate, but according to latest reports she was in a hospital, in very poor health. The intermittent presence of fat in the urine and its occurrence only after the severe attack of dyspnea and cerebral disturbance are emphasized by the writer. His suspicion as to the nature of the case was aroused by its similarity to conditions observed in a case of fracture with fat embolism. Great care was exercised in avoiding any possible contamination of the urine from outside sources, and the results as given cannot be questioned. He finds no mention in the literature of fat embolism coming from a chronic bone disease with no apparent trauma, and hence reports the case. M. Field (Jour. Amer. Med. Assoc., Dec. 7, 1912).

Air embolism may not be attended with serious consequences if only small quantities of air are admitted, but sudden death is not uncommon with the entrance of large quantities. In the latter event frothy blood is found in the right heart, and air-bubbles in the branches of the pulmonary artery. Bubbles may also find their way into the capillaries of the brain and heart muscle. It should not be overlooked that gas in the blood after death may be due to *Bacillus aërogenes capsulatus.* The precise cause of death in air embolism is not positively settled, as the results of experiments upon animals are somewhat at variance with the effects observed in man. The usual explanation is that, owing to the resiliency of the contained air, the right ventricle fails to contract with sufficient force to propel the blood forward. As a consequence the left heart does not receive sufficient blood, aortic pressure is reduced, and death results. Another factor may be the sudden dilatation and paralysis of the ventricle.

The fact that the entrance of air into the veins may lead to serious consequences was first observed by Heyden, late in the seventeenth century, but it was not until 1818 that the first authentic record of this accident in man was reported by Beauchêne. Since then the matter has been of great interest, particularly to surgeons and to obstetricians, as most of the reported cases have resulted from operative procedures, especially in the neck, or from the injection of foreign substances into the uterus.

There can be little doubt, as Welch remarks, that many of the cases reported as death from air embolism are based on entirely insufficient evidence. The researches of Welch and Nuttall, and later of Welch and Flexner, on the *Bacillus aërogenes capsulatus* made it very evident that in future all reports of air embolism must show that the possible action of this gas-forming organism was excluded. Especially in cases of so-called air embolism follow-



Gangrene Due to Thrombus.

ing uterine manipulation, the evidence, in most instances, favors infection rather than the introduction of atmospheric air. Still, all doubtful cases excluded, there can be no question that the introduction of air into the veins does in some instances cause alarming symptoms and sometimes death. Editorial (Jour. Amer. Med. Assoc., April 22, 1905).

Case of death from air embolism, introduced through the uterine sinuses, and not due to gas-forming bacteria. Very sudden death occurred, though the woman was previously in perfect health. It was due to that fact that a syringe containing air and water under pressure was used, the nozzle closely fitting the os. There was a large quantity of air in the dilated uterus and Fallopian tube. Black fluid blood filled the venous system, the arteries being comparatively empty. The heart was flaccid and contained blood admixed with air, which was also found in other organs of the body. No air was found in the placental tissue nor in the cord, nor in the fetus. Holyoke (Boston Med. and Surg. Jour., Dec. 20, 1906).

In a fatal case reported by the writer the air embolism was due to partial detachment of the placenta during the progress of the labor. The child was dead when delivered, and the mother died half an hour after the labor with all the symptoms of cardiac distress due to air embolism. A careful examination of the uterus failed to disclose a rupture. Apfelstedt (Zentralbl. f. Gynäk., Nu. 17-26, 1907).

In a man of 47 being operated for abscess of the lung, there was little hemorrhage until suddenly venous blood began to pour out as the superior lobe was being mobilized. The hemorrhage was readily arrested and camphor injected, but the patient died in collapse in three minutes. Autopsy showed embolism of air sucked into the veins as they were opened by the operation. The air must have passed through the veins of the lung into the left side of the heart, and thence into the general circulation. The disturbance in the cerebral arteries was evidently the direct cause of the sudden death. Bencke (Beiträge z. Klinik der Tuberkulose, Bd. ix, Nu. 3, 1908).

Case in which in an attempt to produce an abortion, quinine was insufflated into the uterine cavity, through a soft-rubber catheter. The woman immediately became unconscious and died about fifteen hours later. Death was ascribed to air embolism, gaining entrance by way of the uterine sinus and carried to the right side of heart, producing a thrombus or going still farther by way of the pulmonary artery to the lungs. T. H. Flesher (Jour. Okla. State Med. Assoc., Jan., 1910).

The writer reports 2 cases of air embolism during labor. The first occurred in an apparently healthy woman, who had had one child. Her second confinement was normal in the first and second stages. She lay on her left side in a narrow bed, with a wire mattress, which was depressed in the center. She had a little chloroform during the later stages of delivery and was not turned upon her back until after the child had been born. When the uterus again contracted, the patient suddenly exclaimed that she was dying, became cyanosed, and had a general convulsive seizure. This passed off, and attempts were made to express the placenta, followed by uterine contraction, which caused another convulsion. The following uterine contraction produced the same result, the cyanosis became permanent, and the patient's heart greatly dilated. The placenta was removed by hand and the uterus washed out with saline solution. A pint of **saline solution** was introduced into a vein in the arm, and **strychnine** given hypodermically. The patient gradually improved and ultimately recovered. In the second case, the patient was a primipara and had always been delicate. Delivery was accomplished under chloroform by forceps, the perineum being somewhat torn. After the child was born the uterine contractions produced spasm, with air hunger, and frequency and irregularity of the pulse. Attempts to express the placenta caused uterine contractions and a return of the spasms.

The patient's heart became markedly dilated. The placenta was removed by hand and the uterus irrigated with **salt solution.** No further spasmodic attacks occurred, and slow recovery followed. Campbell (Brit. Med. Jour., Oct. 22, 1910).

Foreign Bodies. — Dust particles and other substances, after entering the lung in respiration and penetrating the tissues, are borne by phagocytes to the bronchial lymph-glands, and thence, after the disintegration of the gland, into the efferent lymph-ducts and the blood-vessels. The gland may rupture into the adjacent veins. In other instances the foreign bodies penetrate into the blood-vessels. They may lodge in the liver, spleen, bone-marrow, and other structures, or, taken up by wandering cells, be discharged from the lungs, tonsils, intestinal lymphatics, or in the bile.

TREATMENT. — Shock is to be combated by the usual measures. The patient should be placed at rest and the circulation equalized, and, as far as possible, coexisting disorders rectified.

Most cases of supposed pleurisy and pneumonia occurring within from one to three weeks after abdominal section, are probably embolic in origin. As to treatment, we should avoid favoring thrombosis, and while advising a **free use of fluids,** avoid milk, calcium salts, and carbonate of magnesia. **Aspirin** will usually relieve pain, but **morphine** may be necessary, and there is no contraindication to its use; **stimulants** are indicated, and, if the breathing is seriously embarrassed, **oxygen** is advisable. The patients should be kept **quiet** for the first twenty-four hours, but after this he should sit up in bed and be allowed to get up as soon as the pain has passed off and the temperature has become normal. Bidwell (Practitioner, Feb., 1909).

Efforts should be directed toward the maintenance of heat and nutrition to the structures involved; secondary inflammatory or septic processes should be controlled on well-established principles. Stimulants, tonics, and hematics will often be required.

Digitalis to sustain the heart action and its propulsive power is very useful. **Hypodermoclysis** or, better, **intravenous injections** of **saline solution** have been very efficient.

In embolism of arteries which can be reached, especially those of the extremities, **arteriotomy** and **removal of the embolus** often prove successful.

Case of embolism of the axillary artery consecutive to a chronic endocarditis in which gangrene of the forearm ensued, necessitating disarticulation at the shoulder, which was done after the oval flap method of Larrey. The patient rallied from the operation, and after a somewhat slow and eventful convalescence, made a complete recovery. Sherwood (N. H. Lancet, Oct. 15, 1904).

Case of **removal** of an **embolus** from the common iliac artery, with re-establishment of circulation. In cases of aseptic embolism immediate removal by division of the artery at the line of the embolism or below it should be resorted to. These emboli produce mere mechanical obstruction, and the circulation is at once re-established by their removal. The symptoms which indicate the occlusion of a large artery are pain, ischemia of the limb, cooling of the surface, and absence of pulsation in the arterial trunk. The number of hours that may elapse before a tissue becomes incapable of restoration has not been definitely determined, but from the length of time a constrictor may be kept on a limb for the suppression of hemorrhage and the vitality of the limb restored, we know that many hours of complete suppression of the circulation is not incompatible with restoration of the life of the tissues. In the removal of septic infarcts there is little to be gained in a practical way, as they are usually multiple. With the infarcts resulting from acute or chronic vegetations on the cardiac valves, good results should be obtained. Even cerebral ischemia should be amenable to this treatment, when due to an embolus arrested in the common or internal carotid by opening the common carotid and aspirating through a catheter; or a subclavian clot by incision of the axillary artery. The writer found aspiration through a catheter a good means of removing the plug. If the catheter is divided on the slant with its end open it can be readily introduced into the artery; unless the embolus is extremely hard it can with suction be drawn into or fragmented by the catheter and thus the artery freed. Incision into the artery at the seat of arrest of the embolus, if it has been there for any length of time, is not an advisable procedure; the artery had better be divided above or below (preferably the latter) the point of impaction of the embolus. A gradual occlusion of the circulation does not produce gangrene in the extremity. The curved needle of the conjunctival type, which has its cutting edge easily rubbed off on a whetstone, is a good type of needle for deep work. After the removal of the Crile clamp or the digital compression there is often considerable oozing through the stitch holes. A gauze compression for thirty or forty seconds will completely stop all this bleeding. Silk should be used and not animal suture, as a clot rapidly forms around the silk, plugging the stitch hole. Murphy (Jour. Amer. Med. Assoc., May 22, 1909).

Only aseptic cases should be operated on, while the **operation** should be quickly carried out. The subject should be young and free from general arterial disorder, and the seat of the embolism be readily accessible. **Massage** of the involved artery has recently been productive of good results in a few cases, but its range of usefulness is limited because it must be practised within a few minutes after the occurrence of embolism. Mosny and Domont (Bull. de l'Acad. de Méd., Dec. 10, 1911).

Even the **pulmonary artery** should be **opened** in an otherwise doomed patient and **Trendelenburg's technique** employed, when the conditions are favorable for operation. The thorax is opened by a transverse incision over the second rib and a vertical incision made over the left sternal border. The triangular flap thus obtained is pulled back and a piece 10 to 12 cm. long of the second rib next to the sternum resected. If more than forty-five seconds are needed to compress and open the artery, it may be clamped laterally, the compression loosened and the blood-stream let through, and again compressed, etc., and the search for emboli continued. In most cases fifteen minutes are available. The embolus can be extracted through a very small opening in the artery.

Of 878 fatalities among the 9727 patients in Körte's surgical service at Berlin during the last four years, 22 of the deaths occurred suddenly and the symptoms indicated pulmonary embolism. The records of these 22 sudden deaths, when analyzed to determine whether the embolus could have been successfully removed, showed that in 12 cases death occurred instantaneously, and yet autopsy in 7 of the 12 revealed embolism in 4, the findings very similar to those in the more protracted cases of embolism. In 1 case a thrombus about 7 cm. long, about the size of a pencil, was found at the bifurcation of the pulmonary artery and it could have been readily removed. The Trendelenburg operation is indicated, therefore, in such cases when conditions are favorable for immediate operation. In 10 other cases the syndrome of the embolism persisted from ten minutes to three hours before the fatal termination. Autopsy revealed embolism in 6 and conditions would have been favorable for operative intervention in 5 cases. In 4 others the assumed embolism did not exist; these 4 patients were about 50 and 70, and were being treated for a broken arm or femur or ovarian cyst, with no threatening symptoms of heart trouble. A syndrome characteristic of pulmonary embolism suddenly developed in the midst of apparently complete well-being, and death followed in from ten to thirty minutes and autopsy disclosed merely brown atrophy or fatty degeneration of the heart. The writer advocates, in case of the onset of the embolism syndrome, **morphine** to tranquilize the respiration, then a preparation of **digitalis** injected into a vein while all is made ready for an **operation,** which follows if these measures fail to improve, unless contraindicated by general condition. Busch (Deut. med. Woch., July 22, 1909).

The writer found, by numerous experiments on the cadaver, that **Trendelenburg's operation to expose** the **pulmonary artery** to remove an embolus is entirely practicable from the anatomical standpoint, although none of the 5 patients thus operated on was permanently cured. In 55 cases of embolus in the pulmonary artery which he had encountered during the last 6000 necropsies, the embolism followed operations on the trunk or legs in 6 of the 35 cases of which the details are known; it followed injuries of the legs in 3 others, varicose disturbances in the legs in 7, anemia and cachexia in 8, and it occurred with a heart defect in 3. In only 6 cases was the diagnosis of pulmonary embolism made during life, and in these cases the embolism proved rapidly fatal. In all the others there was an interval of from half an hour to forty-eight hours between the onset of the symptoms of embolism and the fatal termination. An interval of from three to six hours was the rule, and it is probable that the embolus gradually increased in size or that the embolism occurred in waves. This is evidenced by the transient improvement under **camphor,** and the discovery in the smaller arteries at necropsy of minute emboli evidently older than the big one that proved fatal. The data show thus that the diagnosed embolism proved too rapidly fatal for any operative intervention, and that in the cases with a sufficiently long interval for operative interference to have been successful, the nature of the disturbances had not been recognized. The embolus was generally located in the main trunk of the artery or one of its chief branches, and from the pathologic-anatomic standpoint might easily have been removed. The great difficulty therefore in the way of successful operative treatment of pulmonary embolism is the failure to recognize it in time. Bloody sputum at the beginning of the disturbances is an almost constant symptom. The mechanical factor should be considered in diagnosis, as the embolism occurred almost invariably after sitting up in bed, getting up, changing the dressings, or after the agitation stage of general anesthesia. Ritzmann (Jour. Amer. Med. Assoc., from Berl. klin. Woch., July 17, 1911).

In air and fat embolisms the intravenous injection of warm **saline solution** supplemented by **hypodermoclysis** has been found very effective. The explanation of this action is that the fat and air globules are broken up and washed along.

In his experimental experiences with air embolism, the writer found that the heart was unable to contract over air as the valves are meant to act on fluids and not on air. After the heart action had ceased after injection of air in the jugular vein, he was able to revive it again by direct injection of 0.5 per cent. **saline solution** directly into the right ventricle. Recent publications have shown that these facts may be employed in the saving of life. Schantz, for example, has recently reported good results in cases of fat emboli, from subcutaneous and intravenous infusions of saline solutions. L. von Lesser (Zentralbl. f. Chir., Feb. 26, 1910).

[In view of the fact that death practically always occurs in embolism in important vessels which cannot be reached, **saline solution** should be introduced intravenously in *all* forms of embolism. Duncan and Illman (New York Medical Journal, Dec. 21, 1907) showed that mixing of the body juices with blood was the predominating factor in the production of thrombi portions of which may constitute emboli. If now we recall that the body processes contain coagulating ferment and other substances capable of promoting coagulation, it will be seen that by rapidly increasing the osmotic properties of the blood, as is done with saline solution, and thereby facilitating the passage of detritus and broken-up emboli into the lymphatic system, much will have been done to save a given case. Ed.]

Much can be done to prevent the formation of embolisms. This feature is so completely and satisfactorily covered in a paper by Hugh Crouse (Surgery, Gynecology, and Obstetrics, Dec., 1909) that the following quotation is borrowed therefrom, even though it refers to both thrombosis and embolism:—

"In general the treatment of the thrombi and emboli should be prophylactic, if possible. In Archiv für Gyn., 1908, vol. lvi, page 218, Singer says that thrombi are indicated in surgical cases by a pulse acceleration, unaccompanied by fever, several days before edema and cord-like vessels occur, and that the pulse rate remains high after the temperature returns to normal. Wyder, Richter, and Muhler concur in this opinion, which is opposed by Clarke. Richter (Arch. für Gyn., vol. lxxiv, page 1) says that in 63 per cent. of his cases the pulse rate warned him of the thrombotic development, and that in 34 per cent. he had doubt because of the synchronous fever. Wyder says he no longer undertakes a serious gynecological operation, where edema and a high pulse rate or other signs of a recent thrombi are present provided the general condition sanctions operative postponement. Tabor Johnson says, in operating, one should protect the wound from injury by retractors, avoid roughness, much hemorrhage, retain patient in bed longer, and aid venous return by elevating the foot of the bed immediately after operation. Boise advocates a careful examination of the heart in all contemplated operative cases, and says: 'If the area of dullness is somewhat increased, if the first sound is disproportionately weak, if after exertion the pulse rate is greatly increased, due allowance being made for existing anemia, if there is a history of chronic exhausting disease, we may justly diagnose heart degeneration, whether we detect any atheroma of the peripheral arteries or not; and, if coupled with these points, a blood test shows an excess of calcium salts with chronic anemia, we are justified in taking all possible precautions against the occurrence of emboli.' Krusen advocates blood test for calcium salt excess, for leucocytosis, and the presence of blood-plates. If an excess of calcium salts be found, Wright and Knapp, seconded by Duncan and Illman, Boise and Krusen advocate the use of 36 grains—2.3 Gm.—of **citric acid,** *t. i. d.;* **alcohol** and large quantities of water. Richards advocates **tobacco smoking.** Howard, **alcohol, oxygen, liquid,** and **fruit juices.** Mayos, Murphy, Ries, Boldt, Chanler, Gordon, Currier, and Brothers advocate as a prophylactic agent the **early getting up of the patient,** upon the theory that the heart contractions are less vigorous in a recumbent posture; that the residual blood from insufficient ventricular action is peculiarly liable to coagulation. All of which is in part avoided by the upright position and physical exertion. Bosher says the treatment of the thrombophlebitis is largely negative, consists of **rests, elevation,** and **cotton bandaging.** Patient not to be allowed to make much muscular effort for some time, when it does occur, until after the complete subsidence of all local symptoms. Avoid digitalis; recommends the wearing of **elastic stockings** for quite a time."

[Very few cases of embolism would occur were **saline solution enteroclysis** used more frequently, after cleaning out the intestine. That deficient osmosis has much to do with the pathogenesis of this condition is emphasized by many physiological and clinical facts. Ed.]

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EMETINE is an alkaloid obtained from *Cephaëlis ipecacuanha* (ipecac). Its chemical formula is $C_{14}H_{18}(CH_3)NO_2$, and it is a methyl derivative of cephaëline, another alkaloid found in the same plant. It is chiefly employed as emetine hydrochloride, which occurs as a white, crystalline powder, soluble in water and alcohol; less often as the hydrobromide, which is less soluble, at least 2 c.c. of water being required to dissolve a full dose of the salt (Rogers).

The term emetine is sometimes also taken—and until the work of Paul and Cowley in 1901 was taken exclusively—to signify a mixture of the alkaloids of ipecac, viz., cephaëline, emetine, and psychotrine, which formerly were not clearly distinguished. This mixture of alkaloids occurs as an amorphous, whitish powder, which has a slightly bitter, acrid taste, darkens on exposure, and is only very slightly soluble in water, though more soluble in ether and especially in alcohol and chloroform.

PREPARATIONS AND DOSE.—The hydrochloride or hydrobromide of the true alkaloid emetine may be given hypodermically in amebic dysentery in doses of 1/3 to 2/3 grain (0.02 to 0.04 Gm.). The expectorant dose of emetine hydrochloride is 1/12 to 1/6 grain (0.005 to 0.01 Gm.). A solution of emetine can be safely boiled for a short time, but it is probably best to boil the water first and subsequently dissolve the drug in it. Rogers found that emetine hydrochloride could be given intravenously in full doses without causing depression.

The alkaloidal mixture "emetine" is emetic in doses of 1/12 to 1/6 grain (0.005 to 0.01 Gm.) and its dose as an expectorant is 1/60 to 1/30 grain (0.001 to 0.002 Gm.).

None of these alkaloids is official.

PHYSIOLOGICAL ACTION.—The mixed "emetine" is possessed of strong local irritant properties, and, when ingested, produces an abundant flow of saliva, owing to its bitter, acrid taste, followed by nausea and vomiting similar to that brought on by the whole drug ipecac. Like most other emetic drugs, "emetine" in small doses tends to increase the secretions of the tracheal and bronchial mucous membrane and induce perspiration. It is said to stimulate the liver. Administered hypodermically in large doses it causes not only vomiting, but also later diarrhea, which may be accompanied by so much irritation of the intestinal tract that blood appears in the stools. Albuminuria, cardiac depression, edema of the lungs, collapse and death are the ultimate effects of poisonous doses. Large doses directly depress the heart, though small, therapeutic doses produce no evident action of this nature beyond an occasional reduction of the tension of the pulse. The drug is said, by reason of the cephaëline contained in it, to have a tendency to dissolve the red corpuscles when injected intravenously.

The true alkaloid emetine is much weaker as an emetic than cephaëline (Lowin), and is therefore, for purposes in which the emetic action is not desired, superior to the mixture "emetine," which contains cephaëline. It is an irritant to mucous membranes, like cephaëline, but this does not preclude its hypodermic use. It is a better expectorant, according to Lowin, than the allied alkaloid, cephaëline, and is less likely to irritate the kidneys. Experimentally, it has proven more depressing to the heart than cephaëline, though Rogers has found it practicable to give doses as large as 1 grain (0.06) hypodermically or intravenously in man without causing circulatory depression.

> Even the fullest doses of emetine, given hypodermically, never produce sickness and very rarely even any nausea. It is therefore evident that the emetic action of the alkaloid is a local one on the stomach, and is probably produced by stimulating an excessive secretion of mucus, which is sooner or later vomited. This supposition will also explain the action of tannic acid in lessening the sickness due to ipecacuanha by inhibiting the secretion of mucus. The drug has extremely little depressing effect, and so can be given in full doses in severe cases of dysentery, or even after copious hemorrhages from the bowel, without fear of adding to the shock. Leonard Rogers (Therap. Gaz., Dec., 1912).

> The author injected 4 grains (0.25 Gm.) of emetine hydrochloride at one dose. This produced nausea for several hours, the patient vomiting once. W. Allen (Jour. Amer. Med. Assoc., March 1, 1913).

Maurel, injecting emetine hydrochloride into frogs, observed a contraction of the vessels in their interdigital webs and concluded that the substance is a vasoconstrictor. In the congestive zone surrounding a wound he found that it overcame vascular dilatation and reduced the degree of inflammation. This accounts, according to Maurel, for the results obtained clinically with ipecac in affections accompanied by congestion, notably in the digestive and respiratory systems. The same fact might also explain the well-known paradoxical antemetic effect of small doses of ipecac.

In excessive doses emetine depresses both the central nervous system and the heart. Death, where it occurs, takes place from respiratory arrest.

THERAPEUTICS.—The mixture of alkaloids incorrectly termed "emetine" is rarely employed, as it has no advantage as an expectorant or emetic over the ordinary preparations of ipecac and is far more costly. Very small doses can be used, however, in the early stages of **bronchitis**, and the drug is said to be of value in **diarrhea** in the minute dose of $\frac{1}{300}$ grain (0.0002 Gm.).

> Emetine and cephaëline given separately to phthisical patients, to some by mouth and to others in the form of suppositories. Emetine was given as a freshly prepared 1 per cent. solution, the dose increased drop by drop, the average being 5 or 6 drops. No marked effect on expectoration and cough was noted, and headache and

nausea were frequently reported. Neither alkaloid given by mouth caused diarrhea, and both could be given by rectum in large doses without occasioning vomiting. Their routine use as an expectorant, given by mouth in phthisis, is inadvisable, as their action in this direction is weak. Inhalation and gargling are rather to be recommended, and for this purpose the cheaper tincture or fluidextract of ipecacuanha is to be preferred. P. Zepf (Arch. Internat. de Pharm. et de Thérap., vol. xii, Nos. 5 and 6, 1904).

The true alkaloid emetine was shown by Vedder, of the United States Army, to possess a powerful destructive action on an ameba presumed to be the parasite of tropical dysentery. Further tests by Wherry and by Leonard Rogers, of Calcutta, only served to confirm this discovery, and the last-named observer, to his enduring credit, put this finding to practical use in the treatment of severe cases of **amebic dysentery**, with surprisingly gratifying results. Not only did he find that the large doses of alkaloid necessary to overcome the amebæ could be injected without causing nausea or depression, but the curative effect was so pronounced and immediate as probably to warrant the addition of emetine to our all-too-short list of truly specific remedies, as well as its use for diagnostic purposes.

Emetine in 1:20,000, 1:100,000, and 1:200,000 solutions found to kill a saprophytic ameba after twenty-three and one-half hours' exposure, at 36° to 38° C. None of these dilutions was amebacidal in an hour. Presumably when amebacidal action was manifested the emetine acted on the trophozoites alone, and failure to kill may be attributed to the presence of cysts. Wherry (Jour. of Infect. Dis., March, 1912).

When mucous dysenteric stools containing numerous active amebæ (*Entameba hystolytica*) were placed in a solution of emetine hydrochloride, the amebæ were immediately killed and materially altered in their microscopic appearances by a 1:10,000 solution, while after a few minutes they were rendered inactive and apparently killed by as weak a solution as 1:100,000. Hypodermic administration of emetine hydrochloride in some cases of **amebic dysentery** yielded phenomenal results. It did not produce vomiting, even though in the same cases ipecacuanha given by mouth had done so. Leonard Rogers (Brit. Med. Jour., June 22, 1912).

Rogers usually administers ½ to ⅔-grain (0.03 to 0.04 Gm.) doses of emetine hydrochloride twice daily to adult amebic dysentery patients, but has on several occasions given 1-grain (0.06 Gm.) doses twice and even three times daily without noting any depressing effect. In children about 8 years of age, ⅓ grain (0.02 Gm.) may be given with entire safety. Only exceptionally does severe pain follow the injection, and in most instances there is no local reaction; nausea is very rarely produced. In the most serious cases Rogers has given slow *intravenous* injections of the drug in the same dosage, without observing any depressing effect on the pulse.

In a patient with marked thickening of the cecum, with great tenderness due to local peritonitis, the author gave first ½ grain (0.032 Gm.) of emetine hydrochloride dissolved in 5 c.c. (80 minims) of normal saline, injected very slowly into the median basilic vein, without the slightest depressing effect on the pulse; the same evening he gave ⅔ grain (0.043 Gm.) and a day later a 1-grain (0.065 Gm.) dose in the same way, in addition to several subcutaneous ones.

Although large, black sloughs were being passed, the dysenteric symptoms rapidly cleared up and the right iliac swelling disappeared. The author has also tried giving one or two ⅓-grain (0.021 Gm.) tabloids of emetine hydrochloride by the mouth on an empty stomach, allowing no food or water for three hours before and after it, and found that the drug is generally retained, or if any vomiting occurs it is not until after several hours, when most, at any rate, of the dose has been absorbed. It is thus far easier to administer, and much better retained, than an equivalent amount of ipecacuanha powder. Several cases of fairly mild **amebic dysentery** were cured within four days by this method, although it is less rapid and lasting in its effects than by hypodermic use; for in 1 case a relapse occurred after a few days, which was quickly cured by injections of the emetine salt. Leonard Rogers (Therap. Gaz., Dec., 1912).

The superiority of emetine over the whole drug, ipecacuanha, is well shown in the following table, representing the results noted by Rogers in two series of cases—one comprising 30 patients treated with ipecac and the second including 25 patients treated with alkaloid:—

	Cases treated with ipecac.	Cases treated with emetine.
Died within three days after admission	4	2
Died after three days	7	—
Died of other disorders (heatstroke and cancrum oris) after cure of dysentery	—	2
Discharged in very bad condition	2	—
Discharged not cured	4	—
Discharged cured	13	21
Average number of days spent in hospital by cured cases	16.4	7.2
Average number of days before stools returned to normal	11.4	2.35
Average amount of drug given before stools became normal	406 gr.	2 gr.

The 2 grains (0.13 Gm.) of emetine referred to in the last column represent an amount of alkaloid equivalent to only 180 grains (12 Gm.) of powdered ipecacuanha — additional evidence of the high relative efficiency of emetine. The drug so rapidly kills off the amebæ that apparently moribund patients can often be brought through safely.

The blood and mucus nearly always finally disappear from the stools of an **amebic dysentery** patient within two or three days, four days being the longest period the author has met with. In bacillary dysentery, on the contrary, the drug exerts little or no effect, so that failure of injections of emetine salts to produce a very material improvement in the stools within two or three days affords very strong evidence that the disease is not amebic in origin. The amebæ disappear from the stools in twenty-four to forty-eight hours after emetine injections are begun; so the parasite should always be sought for before the drug is administered. The author has never seen any harm result from the new treatment in bacillary cases; so it can safely be used for diagnostic purposes.

Leucocytosis of from 25,000 to 50,000 or even more is common in amebic disease, and furnishes important prognostic information. Of 10 cases with such high white-corpuscle counts in which ipecacuanha was given, only 2 recovered, while 4 died in the hospital and 4 were taken away uncured, 3 in a bad condition. On the other hand, under the emetine treatment 4 out of 5 similar cases were rapidly cured, the one fatal case showing a count of 61,750 leucocytes, and dying in less than twenty-four hours after admission. Leonard Rogers (Therap. Gaz., Dec., 1912).

Report of 3 cases of **amebic dysentery** in the treatment of which emetine was exclusively employed. The disease was of six months' to two years' standing, but in all the cases a few injections—5 to 7—of 0.4 Gm. (⅔ grain) of emetine brought about a cure. In 2 cases in which the action on the amebæ was followed, it was noted that on the day after the first injection the organisms were no longer motile, had assumed a spheric form, and were vacuolated. C. Dopter (Soc. Méd. des Hôp. de Paris, April 4, 1913).

Case of **amebic dysentery** of over a year's standing and suffering from recurrent attacks every two or three months. In a period of eight days the patient was given 0.3 Gm. (5 grains) of emetine hydrochloride subcutaneously; on each of the two succeeding days he was given a rectal injection of 0.12 Gm. (2 grains) each; finally he received one more subcutaneous injection of 0.06 Gm. (1 grain). Under this treatment the number of stools *per diem* fell from 16 to 2. A few amebæ could, however, still be found. Dufour and Thiers (Soc. Méd. des Hôp. de Paris, April 11, 1913).

Case of a man, aged 46, who had been suffering from **amebic dysentery** for five years, having had an hepatic abscess, which was relieved by operation, and who had finally become reduced to a state bordering on cachexia. Twelve to fourteen stools, containing mucus and blood, were passed daily, and there was an eosinophilia of 10 per cent. Emetine hydrochloride was given in the dose of 0.04 Gm. (⅔ grain) once daily for a week. Abdominal pain disappeared, and the stools were reduced to 4 and became free of amebæ. The eosinophilia, however, persisted and during the succeeding nine days the stools increased to eight or ten, with blood, mucus and amebæ, abdominal tenderness returned, and the previous subjective improvement disappeared. More energetic treatment was then given, 0.08 Gm. (1¼ grain) of emetine being injected daily for a week, then 0.04 Gm. (⅔ grain) for four days more. By the time the last injection had been given there was but one pasty stool a day, the amebæ and eosinophilia had disappeared and considerable subjective betterment had occurred, though the patient's appearance remained practically the same and no gain in weight had been noted. The outstanding features of the case were the length of treatment required and the amount of drug injected—1 Gm. (15½ grains),—which was well borne. E. Job and L. Lévy.

Another author refers to the case of a man who had contracted **amebic dysentery** in Morocco, and upon his return to France had been passing seven or eight stools daily. These, though very soft, were not of the dysenteric type, being free of bloody mucus and of amebæ. There was no colic or tenesmus, and the condition was undoubtedly due to a chronic enteritis, arising through lesions of the small intestine and consecutive to an amebic process of which no trace was present at the time. Emetine treatment was productive of no result, thus showing that the remedy cannot be counted on to relieve non-amebic intestinal disorders, even where these follow amebiasis. Dopter (Soc. Méd. des Hôp. de Paris, May, 1913).

Case of a patient who had amebic **dysentery** during his boyhood in Turkey and eighteen years later, in France, had a recurrence of his old trouble, apparently brought on by an ordinary attack of benign acute diarrhea. After a long period of ineffectual treatment, the amebic origin of the disease was recognized and emetine given to the amount of 0.32 Gm. (5 grains) in a week. The temperature promptly fell, the number of stools decreased until, on the fifth day, there was no movement at all, pain disappeared, and the patient promptly gained in weight. A. Chauffard (Presse méd., May 14, 1913).

That the amebæ may be all killed by emetine so that no relapse will occur, has not been established, but

Rogers observed that in patients who died for any reason (gangrene of the cecum; numerous small liver abscesses) after emetine treatment, no amebæ whatever could be detected in the intestines or liver.

A very severe attack of amebic **dysentery** cleared up as a result of two injections of ½ grain (0.032 Gm.) of emetine hydrochloride on each of three successive days. The patient returned three weeks after leaving hospital suffering from diarrhea, but without amebæ in the stools, and died in three days, left basal pneumonia being found *post mortem.* The upper half of the large bowel was distended and its wall greatly thinned in places and adherent to surrounding structures, while its mucous membrane showed extensive thin scars of healed ulcers, but no recent lesions, and the liver contained a small, encysted abscess; also free from amebæ. Thus three days' emetine treatment had brought about healing of very extensive amebic ulcers and had also sterilized and led to the encystment of a liver abscess. A second patient was apparently cured of a chronic amebic dysentery by 1-grain (0.065 Gm.) doses on three successive days, but returned four weeks later with severe dysentery and died the next day, no amebæ having been found in the stools on his second admission. *Post mortem,* extensive healed scars of amebic dysentery were found in the upper part of his large intestine, and typical lesions of acute bacillary dysentery in the lower half, from which cultures of Shiga's bacillus were obtained. These two apparent relapses furnish strong evidence that the new method can completely sterilize the body as far as pathogenic amebæ are concerned. Leonard Rogers (Therap. Gaz., Dec., 1912).

In **amebic hepatitis** the emetine treatment has proven nearly as great an advance as in amebic dysentery. Injected in the same doses as in the latter condition, emetine will remove the pain of acute hepatitis in a single day, reduce the fever in a few days, and where abscess formation has not yet taken place, bring about subsidence of the leucocytosis (Rogers). Several French observers have fully confirmed the statements of Rogers concerning the benefit of emetine in this condition.

Report of cases of **amebic liver abscess** treated by aspiration and injection of emetine into the cavity, with uniformly excellent results and the complete avoidance of secondary pyogenic affection of the cavity, which is the common result of open drainage. Leonard Rogers (Brit. Med. Jour., Aug. 24, 1912).

Where leucocytosis in **amebic hepatitis** persists for some time after the pain and fever have subsided under emetine, it is highly probable that an hepatic abscess is present, which had formed before the treatment was begun. In that case it is usually only necessary to remove the pus by aspiration, and to inject 1 grain (0.065 Gm.) of emetine hydrochloride dissolved in about 1 ounce (30 c.c.) of water into the abscess cavity through the aspiration cannula before withdrawing it and sealing the puncture with collodion. If a full course of emetine has not already been given, ½ grain (0.032 Gm.) should be injected subcutaneously twice a day for three days, commencing from the day after the aspiration. The pus withdrawn should be examined by culture for bacteria, and if it proves sterile it is highly probable that nothing further will be required, for the amebæ having all been killed by the emetine, the remains of the abscess will encyst. If the abscess is a very large one a second aspiration may be required after a week or ten days.

Where secondary extensive coccal infection has taken place the abscess must be opened and drained.

In 1 case in which the pain and fever of a very acute hepatitis subsided under emetine injections, but leucocytosis persisted, 10 ounces of pus were removed by simple aspiration, no more emetine being used, and complete recovery ensued without further trouble, the leucocytosis also disappearing.

Thus it appears quite probable that in the large number of amebic liver abscesses which are free from secondary bacterial infection—85 per cent. of the whole in the author's Calcutta experience—incision and drainage will not in future be often required. Leonard Rogers (Therap. Gaz., Dec., 1912).

Case of extensive **dysenteric abscess of the liver,** which had been discharging through the bronchi for five months. The patient brought up daily a tumblerful of blood-stained pus. In a period of five days six subcutaneous injections of emetine hydrochloride, each of 0.04 Gm. (⅔ grain), were given. They were well borne, causing hardly any pain, and no nausea or diminution of arterial tension.

On the succeeding day the patient already felt distinctly better. The discharge rapidly lost its hemorrhagic appearance and on the sixth day ceased entirely. The temperature fell to normal on the second day, and a rectal ulcer previously noted healed completely. The patient's strength rapidly returned. An X-ray examination showed that the abnormal liver and lung shadow previously observed was gone. A certain degree of leucocytosis alone persisted. Chauffard (Bull. de l'Acad. de Méd., Feb. 25, 1913).

Case of a woman who, after contracting **amebic dysentery,** had been expectorating pus for eighteen months, and was considered to have tuberculosis. Incision of an **hepatic abscess,** with complete evacuation of the pus, caused prompt and marked improvement, terminating in apparent recovery. But a month later the purulent expectoration recommenced. Another operation yielded only a temporary result, cough and fever persisting. Four injections of emetine hydrochloride—the first two of 0.08 Gm. (1¼ grains) and the others 0.06 Gm. (⅚ grain)—were then given on successive days. On the day of the last injection the fever and discharge were already markedly reduced, and further improvement followed.

About a month after the above treatment, however, the temperature rose to 38° C. (100.4° F.), and the pus became brown again. A second series of four injections of 0.08 Gm. (1¼ grains) was then given. Improvement was as rapid as after the first series, and a month later the patient seemed completely cured and had resumed her usual occupations. Radiography of the right base yielded a normal picture. Flandin and Dumas (Soc. Méd. des Hôp. de Paris, March 7, 1913).

Case presenting a large **hepatic abscess,** which had developed some months after an attack of diarrhea devoid of any special features. Upon incision a liter of sterile pus, containing numerous amebæ, was evacuated. The temperature fell, but an abundant purulent and hemorrhagic discharge took place along the drain. Five days after the operation, 0.04 Gm. (⅔ gr.) of emetine was injected under the skin, and on the next day 0.02 Gm. (1¼ grains) in 40 c.c. of water was injected into the abscess cavity.

Finally, on the two succeeding days, another hypodermic injection of 0.04 Gm. was given. After the first injection the pus was already less blood-stained; after the third it contained no more blood and was much less in amount; four days after the last injection, it had entirely ceased and the temperature was normal. A. Chauffard (Soc. Méd. des Hôp. de Paris, March 14, 1913).

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EMPHYSEMA, PULMONARY.

—**DEFINITION.**—A relative increase in the amount of air in the whole or part of the lungs. This may take place in the interlobar structures, which normally do not contain air, or may occur as a result of distention of the infundibuli and alveoli, with atrophy of the alveolar walls.

[The term emphysema as originally employed was used to express an inflation of the areolar tissues of the body with air, and in that sense it antedated Laennec. To Laennec, however, who first applied the term according to the above definition, we are also indebted for the first, clear, anatomical and clinical description, stamping the disease as comparatively frequent, definitive, and a readily recognizable entity. Ruysch and Valsalva, Morgagni, and Dr. Baillie had all noted "cellular dilatation" occurring in the lung, and in the "Treatise of the Asthma," published by Sir John Floyer in 1698, he quaintly describes the lung of a horse that had been "broken winded," and gives an excellent account of the pathology, clinical course, and even cites many of the etiologic factors accepted today. He then applies these facts to the human. He says, "As it happens in external flatulent tumors, they at first go off and return, but at last fix in permanent flatulent tumors; so it is in the flatulent asthma, the frequent nervous inflations induce at last a constant windy tumor or inflation; and it ought to be considered how far holding the breath in hysteric fits, or the violent coughing in long catarrhs, or the great distention of the lungs by an inflammation in the peripneumonia, may strain the bladders and their muscular fibers, and thereby produce the same rupture or dilatation or hernia as happens in the broken winded. This must be observed by the help of the microscope; and if the air blown into any lobe will not be expelled thence by the natural tone or muscle of the bladders, that the lobe may again subside of itself, 'tis certain some injury is done to the ventiducts; the bladders are either broken, and admit the air into the membranous interstices, or else they are overdistended like a hernia in the peritoneum; and this will produce an inflation of the whole substance of the lungs, and that a continual compression of the air and blood-vessels, which will produce a constant asthma." W. E. ROBERTSON.]

VARIETIES. — Emphysema may be divided into:—

1. *Interlobular,* extra-vesicular, extra-alveolar, or interstitial emphysema.

2. *Vesicular* or alveolar emphysema; alveolar ectasia. This variety may in turn be divided into (*a*) Acute vesicular emphysema; (*b*) Compensatory emphysema, focal or diffuse; (*c*) Hypertrophic or large-lunged emphysema; (*d*) Atrophic or small-lunged emphysema.

1. Interlobular Emphysema.—This variety is due to the rupture of air-cells; the air escapes into the interlobular and subpleural connective tissue. The air fashions bead-like prominences, arranged in rows or groups, or they may occur as large bullæ and are movable under the pleura. Rarely, when the rupture occurs near the root of the lung, the air will escape into the mediastinum, infiltrate into the tissues of the neck and thorax, giving rise to a more or less diffuse cutaneous emphysema. Spontaneous pneumothorax, with or without pleuritis, may arise more or less suddenly even in a healthy person, due to rupture of a subpleural vesicle. Rarely, a râle simulating a fine, pleural, friction rub may be heard.

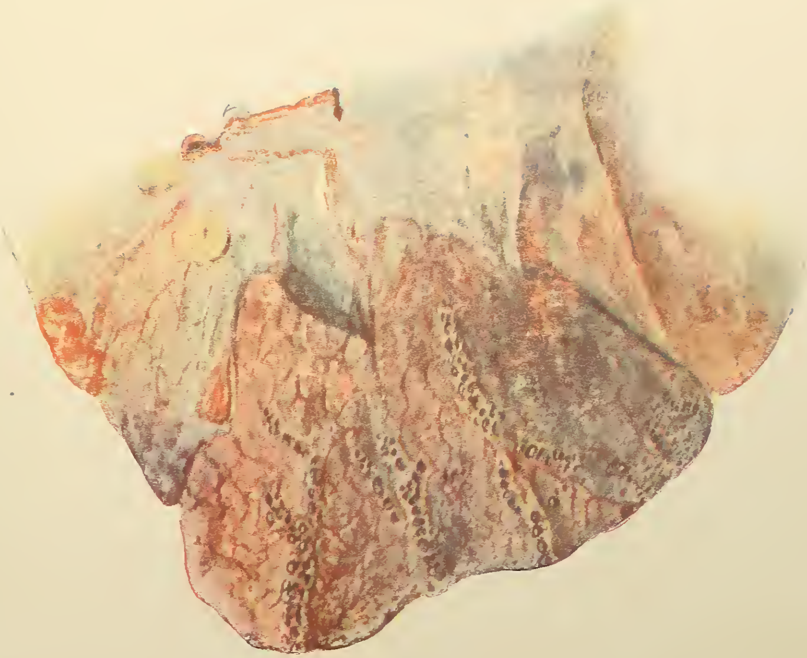
2. Vesicular Emphysema. — (*a*) *Acute Vesicular Emphysema.*—This is due to overdistention of healthy alveoli without atrophy of the alveolar walls. It is apt to occur as part of an acute bronchitis in bronchopneumonia or asphyxia, with violent inspiratory efforts, and totally to disappear with the recovery of the patient from the primary condition. In cases of cardiac asthma and angina pectoris it may also occur. The area of pulmonary resonance is increased and numerous small, diffuse, musical râles heard. Thus, pressure on the vagi by enlarged glands may give rise to a similar condition.

(*b*) *Compensatory Emphysema.*—This is limited to a single small focus or may be widespread, even involving an entire lung, dependent upon the size and nature of the provocative lesion. If any part of the lung area does not fully expand during inspiration, some other portion of the lung will overdistend, or in time the chest wall will sink in order to fill in the space thus created. At first this is a physiological process, but in time atrophy of the alveolar walls takes place; contiguous air-cells fuse and fibrous tissue proliferation ensues. Partial or complete arrest of tuberculous foci or cavities, pleural adhesions and cirrhosis of the lung, all give rise to this condition; likewise pleurisy with effusion, especially if of long standing; also pneumothorax. In proportion to the extent of pulmonary disablement, emphysema arises, so that an entire lung and even part of the second may become involved.

(*c*) *Hypertrophic Emphysema.*—This condition, known also as idiopathic or substantive emphysema, was called by Sir Wm. Jenner large-lunged emphysema. The term hypertrophic is really a misnomer, as there is a diminished and not an increased functional activity. Clinically the disease is easy of recognition. The thorax is voluminous, due to the pulmonary distention; and dyspnea and especially cyanosis are, sooner or later, very pronounced.

MORBID ANATOMY.—In interlobular emphysema more than in any other form, heredity plays a part; it is probable that some subtle tissue change pre-exists, probably a congenitally low grade of elastic tissue. In consequence, overdistention rapidly manifests itself, whatever the cause or even without apparent cause.

When the thorax is opened it will be noted that the costal cartilages are calcified, and even in children this is apt to be the case. According to Freund this primary change in the cartilages brings about a rigidly dilated chest with a secondary large-lunged emphysema. The lungs do not collapse even when removed from the body. They are pale (pulmonary albinism of Virchow), due to absence of pigment in parts; soft, downy, noncrepitant, and pit on pressure. In some instances the lobules are circumscribed by pigment. Distended air-vesicles may be seen beneath the pleura, varying in size, the largest along the free margins of the lungs. An inflated lung, dried and sectioned, will show these to consist of intercommunicating cavities, dilated alveoli, with atrophic septa and vessels and fibrous tissue. The lung looks bloodless and is dry, unless a hypostasis or pulmonary edema has occurred at the bases, due to cardiac insufficiency. The bronchial tubes are the seat of chronic changes, thickening and swelling of the mucosa of the larger tubes, with at most but a moderate bronchiectasis of the smaller tubes, if at all, except in cases of interstitial pneumonitis—pulmonary cirrhosis—where the peribronchial fibrosis invites a more marked bronchiectasis. Mucopurulent secretion is found in the bronchi. Pleural ad-



Pulmonary Emphysema.

hesions are the exception. Rupture of dilated vesicles predisposes to pneumothorax; but if the pleura remains intact, interlobular emphysema results.

> The anatomical changes in the lung cannot be held responsible for the development of emphysema, because in a great number of the cases no anatomical changes are demonstrable, notwithstanding the marked lung distention. On the basis of his clinical studies and observations the writer is able to show that anatomical changes are not essential to the production of emphysema, and, further, that it is produced as a result of the changes in the shifting of the mechanism brought about by air hunger, *i.e.,* because of functional changes. Too much air is inhaled for that expelled, and emphysema results from excess of residual air. Hofbauer (Deut. med. Woch., Aug. 15, 1912)

Owing in part to pressure and in part to stretching exerted by dilated air-cells, and in some measure to fibrous tissue proliferation and contraction, the pulmonary and bronchial vessels are narrowed even to obliteration, and lymphatic circulation is likewise impaired. This necessarily increases the vulnerability of the pulmonary tissue and increases the tendency to bronchitis and pulmonary inflammations.

The right heart feels the strain, the right ventricle and auricle become hypertrophied and dilated, the tricuspid orifice widens, the venæ cavæ enlarge, and congestion of all the organs drained by them results. To a less extent the left side of the heart is involved. Owing to the great increase in volume of the lungs and the depression of the diaphragm, the heart lies lower and more horizontally than normal, the anterior face of the organ being then made up entirely of the right ventricle and auricle.

The mitral and tricuspid valves often become fibrotic, less often the aortic, and the pulmonary artery is invariably the seat of atheroma, more or less marked.

The liver enlarges, is congested, indurated, "nutmeg" on section, and the hepatic veins are dilated. The kidneys are cyanotic, indurated and usually the seat of a chronic, interstitial change. The spleen dense, cyanotic, and moderately enlarged. In the stomach and intestines are present more or less catarrhal change due to chronic, passive congestion.

SYMPTOMS.—Pathologic changes in the lungs may be advanced before the patient is conscious of any particular abnormality. Without any apparent cause, or after an attack of bronchitis or some one of the factors previously cited, some dyspnea is noted, at first on effort. The longer the myocardium is able to compensate, the more slowly will the disease progress. Anything which interferes with the descent of the diaphragm, as overfeeding, or occupations requiring stooping or crouching, or flatus, will render the pulmonary change more apparent by increasing the dyspnea. With this are closely associated, cough and cyanosis; at first, like the dyspnea, intermittent; later, almost constant, at which time orthopnea prevails. Harsh, wheezing respiration, with prolongation of expiration, aggravated by colds and intercurrent bronchitis, and attacks of dyspnea and cough, with or without cyanosis, are the only symptoms for a variable length of time. These symptoms are more marked in winter than summer, the winter bronchitis and cough being especially troublesome. Finally, these conditions persist throughout the year, with periodic attacks of asthma. In early life, this may go on from year to year with but little change, often two or more members of a family being affected, more often the males; but with advancing age the more frequently recurring attacks of bronchitis stamp the sufferers indelibly.

It is the strain incident to coughing that taxes the circulation and hastens decompensation. Cyanosis then becomes more or less constant, and in some cases is quite as marked as it is in congenital heart disease. It may even be quite pronounced while the patient is able to be about. One seldom sees cyanosis so striking under any other condition in one who is up and about. In poisoning by the coal-tar group a similar state of affairs exists, but with the same degree of cyanosis in heart disease the patient is orthopneic.

> Observations affording direct evidence that the patients suffer from impaired ventilation of the pulmonary alveoli, with consequent high carbon dioxide content of the alveolar air, rather than from a deficient intake and absorption of oxygen. None of the cases studied showed the slightest modification of the symptoms when pure oxygen was inhaled. C. F. Hoover (Archives of Intern. Med., Jan., 1913).

The moderate anemia existing is masked by the polycythemia. In consequence of the overfilling of the venous system, the arteries are poorly filled and the pulse is small and weak. The heart is irregular, intermittent, and in the later stages the blood-pressure is low. The cervical veins distend, often filling from below, even pulsating, showing incompetent jugular valves, with dilated right heart and incompetent tricuspid orifice. Marked epigastric pulsation occurs, due to the abnormally low and transversely situated heart.

> The "epigastric pain-point" is common in pulmonary emphysema. It is usually located in the immediate vicinity of the xiphoid cartilage. Pressure upon the epigastrium increases the pain and sometimes makes it intolerable. It is frequently an early subjective phenomenon in pulmonary emphysema and was seen in five-sevenths of a series of cases of that disease. The pain is not necessarily associated with arteriosclerosis, though it sometimes is. It is probably due to some morbid condition in the right ventricle of the heart. It is of little prognostic importance in pulmonary emphysema since it is merely a symptom of the initial condition of the disease. H. de Buen (Revue de méd., Dec., 1905).

Hemoptysis is not uncommon, but, as in mitral stenosis, the amount of blood lost is usually small. Fatal hemoptysis is rare. Expectoration never results from the emphysema alone, but is due to the associated bronchitis, and is proportionate thereto. In the earlier stages the sputum was described by Laennec as pearly, later increasingly profuse, and mucopurulent to purulent.

Deficient aëration of the blood induces headache and drowsiness. The appetite is poor, tongue coated, bowels constipated, and flatulence and distention are not only annoying, but interfere with the action of the diaphragm and further embarrass respiration.

The physiognomy is striking. Early, the rounded shoulders, forwarded position of the head, thick lips, congested mucosa, barrel-shaped thorax and later, with loss of flesh, the same pose with evident embarrassment of breathing, the voluntary muscles being employed; the careworn, anxious expression; cyanosis, prominent eyes, injected veins, clubbing of fingers and toes confined to the soft tissues of those parts, prominent abdomen, epigastric pulsation, low position of liver and spleen, gastrointestinal catarrh and, in time, edema of legs, later becoming general, with effusion into the serous cavities. The course of the disease is afebrile unless pneumonia supervenes.

Physical Signs.—*Inspection.*—For a more or less extended period no striking physical signs can be elicited. Possibly a rather resonant note over the lungs, but eventually, though very gradually (less so in those in whom marked hereditary predisposition is a factor), all of the characteristic signs develop. The most notable is the change in shape of the thorax. This becomes rounded, the anteroposterior diameter increasing, often to a greater size than the transverse diameter. The lower portion of the chest is especially voluminous, the interspaces widened; the intercostal angle becomes more obtuse as the ribs assume a more horizontal position. The sternum acquires a forward bend from above downward, and both sternum and costal cartilages are often prominent features. The neck is short, and owing to the play of the voluntary muscles during inspiration the entire thorax is lifted during the respiratory act, while the sternal fossæ appear unduly deep. There is actually very little increase in expansion, though the effort during breathing is exaggerated. Inspiration is short while expiration is prolonged. Abdominal movement may be inverted during inspiration, the upper portion being retracted instead of distended. Dilated venules are commonly present over the lower thoracic region, along the line of attachment of the diaphragm. Epigastric pulsation is marked; the apical impulse feeble or absent. The cervical vessels are overfilled, prominent, and in some instances pulsate. At this stage, more or less constant, often profound cyanosis is present, increased during coughing or other effort. The spine is curved anteroposteriorly, the shoulders rounded, giving a thick set to the figure. The scapulæ tend to assume a horizontal position.

Palpation confirms inspection as to the character of respiratory movement, feeble or absent apex beat, forcible epigastric impulse, and, further, elicits an enfeebled vocal fremitus. With an associated bronchitis, a rhoncal fremitus may be felt.

Percussion.—Markedly hyper-resonant note, even tympanitic, over the entire chest, often masking cardiac dullness, unless very light and superficial percussion be practised, extending abnormally low, the distended lungs displacing the diaphragm and abdominal viscera downward, and partially obliterating liver dullness.

Auscultation.—Over the lungs the inspiratory note is soft, feeble, short, while the expiratory element is prolonged, often harsh, and owing to the frequency of an associated bronchitis, apt to be obscured by râles, both mucous and sibilant. All other breath sounds may be replaced by râles. Cardiac sounds are feeble, with more or less relative accentuation of second sounds except the pulmonic second, which is absolutely accentuated. In the later stages, when decompensation has set in, murmurs develop, especially that of tricuspid regurgitation, though a mitral systolic is not uncommon.

Course and Duration.—The hypertrophic or large-lunged type of emphysema is a slowly progressive malady, often beginning during childhood, punctuated by attacks of bronchitis, recurring with gradually increasing frequency, often asthmatic attacks, death resulting from some intercurrent pulmonary disease, as lobar or lobular pneumonia or, occasionally, hemoptysis, due to ulceration of the bronchial mucosa, or progressive cardiac failure. The total duration is a matter of years, but in those in whom the disease began in childhood life is seldom prolonged beyond middle age, and death not seldom occurs in early adult life. At best, the victims are semidependent members of society, for respiratory or cardiac embarrassment, or both, preclude useful effort.

(*d*) *Atrophic Emphysema.*—Small-lunged emphysema, so named by Sir Wm. Jenner, is essentially a senile change, an atrophic condition, part of a general wasting process. The need of respiratory interchange is therefore lessened, and, in consequence, the restriction of pulmonary area is clinically less apparent.

These cases are characterized by bronchitis and cough, which often tends to recur solely during the fall and winter months. These symptoms, with the resulting dyspnea, may recur for years or, in some cases, they may be present constantly, but increase in severity during the fall and winter seasons. Bronchial asthma is the exception in atrophic emphysema. Venous congestion, clubbing of the fingers and toes, and cyanosis do not occur.

Physical Signs.—*Inspection.* — The skin is harsh, dry, wrinkled; the muscles wasted; the thorax is small, but often barrel shaped, due to shrinkage, especially lateral. As the lungs gradually occupy less space, the ribs recede and become more oblique. The upper four or five interspaces may be fairly well marked, but the lower ones are crowded by the increasing obliquity to which the lower ribs are especially liable.

Respiratory excursions are much limited; the rigid thorax moves as one piece, but the disproportion between intake and output of air is less than in the hypertrophic form. The heart is apt to be considerably hypertrophied, the apex beat displaced in proportion, less from the emphysema directly than from the vascular and renal sclerosis which are part of the picture. Epigastric pulsation is not increased, —in fact, is rarely present.

Palpation.—This affords confirmation of inspection and feeble or absent vocal fremitus. The blood-vessels are firm, often sclerosed and beaded.

Percussion.—The note is apt to be more tympanitic than that elicited in the large-lunged variety. The precordial area on light percussion will be found increased. There is no displacement downward of the abdominal viscera, nor is the liver dullness obliterated.

Auscultation.—Weak breath sounds with somewhat prolonged expiration. A few small, moist râles can usually be heard at the bases posteriorly, and when bronchitis is present small mucous râles dominate all other sounds. Heart sounds are usually feeble, especially the muscle element, and the pulmonic second sound is rarely accentuated very much.

DIAGNOSIS. — The interlobular form is rarely recognized during life. It may occur after tracheotomy, or in punctured wound of the lung, but its presence may be suspected if subcutaneous emphysema is present, or when pneumothorax develops suddenly after a violent attack of coughing or severe strain. The fine, crackling râle, said to occur in some instances, may possibly be of diagnostic value. Acute vesicular emphysema is an intercurrent affection of rapid onset, a possible complication of severe forms of cardiac asthma or stenocardia. Expiration is prolonged, numerous small râles are present, and a markedly hyper-resonant note can be elicited over the voluminous lungs.

Compensatory emphysema, a frequent sequence of pulmonary tuberculosis, may be suspected in that condition. It is worthy of note that loss of function of a more or less extensive area of lung tissue, may be followed by a true hypertrophy of the remainder, increased functional capacity resulting in the uninvolved areas. In such cases, the breath sounds are harsh, bronchovesicular. Usually, however, emphysema occurs in those portions of the lung not the seat of fibrosis or softening. In such areas, the note is hyper-resonant and the breath sounds soft and distant, with diminished fremitus. In this form, examination of the sputum for tubercle bacilli is very important.

Emphysema in the apex of the lung is most common in the chronic fibrous cases with comparatively slight tendency to destructive processes. The tuberculous focus generally develops about an inch below the apex, and consequently there is a zone of sound tissue above. Assumption of emphysema in the apex explains the clearing up of an area of dullness without this being necessarily a sign of healing. Orszag (Berl. klin. Woch., Oct. 14, 1912).

The large- and small- lunged types are so characteristic that little remains to be said of them in a diagnostic sense. The history, chest conformation, and physical signs furnish data of most importance.

Pneumothorax is occasionally mistaken for hypertrophic or essential emphysema. It is unilateral, however; the affected side bulges and is almost or entirely fixed; the interspaces are filled out without an increase of tension; the heart is displaced to the sound side; the percussion note is tympanitic in proportion to the degree of intrapleural tension, up to a certain point, beyond which, when the tension is at the maximum, the note will be dull or even flat. Fremitus is absent over the affected side and the breath sounds are either wanting entirely or may be heard feebly, possessing a metallic, tinkling quality. The coin test may also be elicited.

Rarely, cases of *failing right heart* with pulmonary edema; large, moist râles; frothy, mucous expectoration, often bloody, may be mistaken for essential emphysema. This is most likely in cases of mitral stenosis or chronic interstitial Bright's, where dilatation has superseded hypertrophy. Of course, in the late stages of emphysema, cardiac failure is superadded and similar symptoms may result. Several days may have to elapse before the differential diagnosis is possible. Atrophic or senile emphysema seldom presents any difficulty in diagnosis.

In certain cases emphysema is only apparent, the cases being in reality

> dyspneic dyspeptics, with a small thorax and a large abdomen. This may be elicited by a clinical study and radioscopy. The thorax is made smaller by the rising of the diaphragm, due to the excessive abdominal mass, which results from gas and aërophagia and the exaggerated tension of the abdominal parietes the muscular coat of which is doubled by a thick coat of fat—all such subjects being obese. This false emphysema is readily curable. Caussade and Leven (Presse méd., April 13, 1912).

ETIOLOGY.—Emphysema occurs at any age, most commonly, however, in late adult life, especially the atrophic form, which is usually senile. The hypertrophic variety is the form most commonly met with in the young. It is most frequently met with among men, in large measure owing to their occupation and greater liability to muscular strain, exposure, etc.

As to heredity, the hypertrophic form may be spoken of as a family type, the quality of vital tissue transmitted, so to speak, being such as to predispose to emphysema. Both in this form and even more so in the atrophic form, vascular and renal degeneration (sclerosis) are common. The hypertrophic form met with in children is very apt to exist without any history of an adequate exciting cause, and even before the disease is well developed, the child lacks animation, tires readily, and manifests little desire for the more active sports of childhood. Capacity for work, though in large measure dependent upon structural differences in individuals, is not susceptible of proof, grossly or minutely, and it is this subtle difference in tissue quality, and especially in the elastic tissue, that invites in one an emphysematous condition, while another escapes.

Muscular effort is the predominating occupational factor, and even those trades involving the inhalation of dust are chiefly harmful in consequence of the associated bronchitis and cough thereby induced. Anything, therefore, which necessitates severe muscular effort, invites the possibility of emphysema, and this possibility is greatly enhanced by certain family types. Porters, stevedores, and laborers are more susceptible even than players of wind instruments. Especially liable are grinders, stonecutters, and coalminers, owing to the irritation of the bronchial tract.

> In 22 players of wind instruments, and a number of other persons, there was found a tendency to overdistention of the upper part of the lungs. Diffuse chronic emphysema, however, is generally the result of disturbances in breathing caused by chronic inflammatory narrowing of the bronchi. E. Becker (Beiträge z. Klinik der Tuberkulose, Bd. xix, Nu. 2, 1911).

Certain diseases are apt to be followed by emphysema, as whooping-cough, chronic bronchitis, asthma, and any factor which lowers pulmonary elasticity, as chronic heart disease or advancing age. Pneumonia, pleurisy, and tuberculosis are prone to give rise to focal or circumscribed varieties of vesicular emphysema.

Traumatic Emphysema.—Traumatism is most apt to invite the interlobular or subpleural varieties. Rupture of the air-cells permits the escape of air into the interlobar or subpleural tissues. Injury to the lung, as in some cases of fractured rib, punctured wounds of the thorax, violent strain as in weight lifting, paroxysmal cough, and rarely during convulsions, parturition or defecation.

Emphysema as a complication during labor is rare. In a case that occurred at the Sydenham Hospital in New York, during the acute stage of labor, a swelling suddenly appeared on the right side of the neck and face. Before the completion of the labor it had extended to the root of the neck and upper part of the chest. The eye of the affected side was completely closed up.

It disappeared within ten days and there were apparently no other abnormal symptoms.

Similar instances of emphysema have been known to occur from excessive vomiting or paroxysms of coughing. This complication is rare; Kosmak in 1907 could collect only 77 cases in the literature since 1791. It occurs almost always in primiparæ and no anatomic explanation is given of the cause of the rupture of the air-cells.

The prognosis is always good; the treatment symptomatic and expectant. M. J. Siegelstein (Jour. Amer. Med. Assoc., July 22, 1911).

Two cases of extensive emphysema developing from rupture of a cavity in the lung or wound of the lung from a fractured rib. The patients suffered greatly from the general diffusion of air, threatening suffocation, until he introduced an ordinary puncture needle to which a rubber tube was fastened, the outer end of the tube resting in a vessel containing an antiseptic solution. The relief was immediate, the escaping air bubbling up through the fluid and the distended tissues subsiding into place; the patients succumbed to the original or primary disease without having suffered through their emphysema. Brondi (Gaz. degli ospedali, Feb. 29, 1912).

PATHOGENESIS.—Two theories have long prevailed concerning the pathogenesis of emphysema, viz., the inspiratory hypothesis and the expiratory hypothesis.

Inspiratory Hypothesis.—The earlier view, originally promulgated by Laennec, regarded the inspired air as the distending force, its egress being hindered by bronchial mucus or swelling of the bronchial mucosa.

Sir Wm. Gairdner, in 1850, looked upon some change in the lung, as collapse or a retrocedent tubercle, as a necessary precedent of emphysema. A reduction in size of one part of the lung thus caused strain upon other parts. These views, however, are no longer given credence.

Expiratory Hypothesis.—Mendelssohn, in 1845, was the first to claim that forced expiration is the chief factor in the production of emphysema. Not cognizant of this at the time, Sir Wm. Jenner, in 1857, announced the same view, but in his article in Reynolds's "System of Medicine," he gives due credit and further states that "Mendelssohn's paper was unknown in this country (England), and rarely, if ever, referred to abroad till Biemer's article appeared in 1867. Jenner states that "The lung during expiration is compressed at different parts with different degrees of force. The parietes of the thorax in consequence of their anatomical constitution, yield to the same force at different parts with various degrees of facility.

"The chosen seats of emphysema are exactly those parts of the lung which are the least compressed during expiration and which are situated under those parts of the thoracic parietes that give way the most readily before pressure." Any extra effort made at the end of inspiration, when pulmonary tension is at its height, especially when the glottis is closed, forces the air centripetally, and the peripheral portions of the lung least supported suffer most; hence we find the lungs most apt to be emphysematous at the apices, and along the anterior margins of the lower lobes and the margins of the extreme base, this latter, especially on the left side, as the stomach area is less resistant than the region of the right lobe of the liver.

Hence the cough, especially resulting from bronchitis, and repeated muscular strain of any kind, increase intrapulmonary tension. If the quality of tissue be good, no harm may follow unless the exciting factor is operative over a considerable period of time.

It is thus quite comprehensive that an acute vesicular emphysema or even interlobular emphysema may occur, recovery being proportionate, especially to the inherent quality of the elastic and muscular tissue. In asthma the changes are more gradual. Bronchial obstruction causes at the same time increase in expiratory effort and an increase in the quantity of residual air. Likewise laryngeal obstruction, be the cause what it may. Necessarily, in time, compression and distortion results in further obstruction of the bronchi and more or less vascular obstruction, and thus a lowered nutritional state results, predisposing the lung to a further yielding.

TREATMENT.—Emphysema as a disease entity is not known to the laity. It is not the emphysema as such for which the patient seeks relief, but the associated bronchitis which is an inevitable phase of the well-developed form. Just as is the case in the earlier stages of cardiac decompensation, so in emphysema, the shortness of breath (at first only on effort) does not constitute sufficient ground for annoyance or discomfort, as in both of these conditions the individuals become more or less accustomed to it.

> The writer examined in 1878 a country messenger 33 years old for life insurance, and advised special rates because of moderate emphysema and the fact that the applicant had to do a good deal of hill climbing. The company refused the application. The applicant continued at his work, and thirty-four years later the writer was called to treat him for trouble in walking, weakness, etc. He found him suffering from a high degree of arteriosclerosis, but the patient, then 67 years old, showed almost the same degree of emphysema as on the first examination for insurance. This case taught the writer not to be too fearful of recommending applicants with emphysema for life insurance. Keller (Blätter f. Vertrauensärzte d. Lebensversicherung, March and April, 1912).

In the young who have sustained acute overdistention, as a result of spasm, whooping-cough or some laryngeal or bronchial affection, the process subsides with the recovery from the provocative factor.

In the *hypertrophic form,* even in childhood, when once thoroughly developed, or in the *atrophic form* in later life, very little is to be expected, indeed, if anything, from any plan of treatment. Some effort should be made, chiefly through regulating the life of the individual, to prevent the resultant effects upon the circulatory apparatus. More, however, may be done in a preventive way, through change of climate or occupation. Any effort which induces shortness of breath should be restricted as far as it is possible to do so. Unfortunately, since patients do not present themselves until some one or other of the complications or sequels of emphysema make it urgent, it is frequently impossible to render any considerable degree of benefit.

The principle underlying therapy is the removal of residual air; consequently some form of aërotherapeutics may be employed, the patient breathing into the rarefied air. This plan has been followed by Dr. Fowler, who, however, believes that the results are not so satisfactory as the employment of what he terms **compressed air baths.** These he has used at the Brompton Hospital with considerable success. He states that breathing is greatly facilitated, while in the bath, and that capacity for exercise materially improves after a series of them have been taken; also the cough and amount of expectoration are greatly lessened. This method, however, is not generally applicable.

> In 6 patients under treatment by **respiratory exercises,** first case a man of 49 had bronchitis every winter, accompanied with dyspnea and cyanosis when the patient was first seen. After 42 *séances* of respiratory therapy in the course of seven weeks the lung capacity increased from 3000 to 4000 c.c. while the dyspnea and cyanosis disappeared. The excursions of the thorax increased from 1 to 5 cm. Haus (Norsk Magazin f. Laegevidenskaben, lxii, No. 5, 1906).
>
> The writer uses a contrivance which presses in the abdominal wall—an air-filled cushion under an inelastic band. The cushion is inflated to exert pressure just at the end of expiration; it forces up the relaxed diaphragm and the immediate relief is so marked that the patient realizes the advantages from drawing or forcing the diaphragm up as high as possible during expiration, and he learns to utilize his own forces for this. The circulation is promoted at the same time by these breathing exercises to such an extent that the general health is materially benefited. Hofbauer (Wiener klin. Woch., March 28, 1912).

[One of the most useful devices for this purpose is **Rossbach's chair,** which can be worked by the patient or an attendant, and affords great relief. It is of the ordinary modern type without arms and with a straight back. The seat is prolonged backward about three inches and two horizontal brackets, *B,* are attached to the top rail. These support two wooden cylinders, *A,* about three inches in diameter and as long as the back of the chair. They are placed on each side just without its outer rail. These revolve on iron pins which pass through the projection of the seat and the brackets respectively. At the bottom of each is attached a lever or wooden handle of convenient length for the patient to grasp with his arms extended. When drawn forward parallel to each other the cylinders make a partial revolution. A broad band of strong webbing (*F F'*, Fig. 2) passes across the chest of the seated patient and is attached by eyelet-holes to a row of studs, *C,* on the inner face of the two rollers; therefore, on pulling the handles forward the thorax is compressed to any extent which may be thought necessary. The bandage is divided in the middle and is fastened in front as a corset. The patient rests himself in the chair, well back, the levers are drawn outward and the belt adjusted so as to press equally over the thorax, and is fastened to rollers on either side. Extending his arms, he grasps the handles, takes a deep breath, and, as expiration commences, pulls them slowly forward; the act completed, he pushes them somewhat quickly to their first position, takes another deep breath, pulls them gently together again as far as he finds necessary, and so on. Here we have artificial respiration with an automatic operator. These movements are timed and persisted in as long as the physician may direct, fifteen times per minute for ten minutes, three times a day. This instrument equally compresses the chest. The patient can use it when once adjusted, either day or night. Any carpenter can make it at little expense. It can be used simultaneously with other forms of treatment, such as Waldenberg's cabinet, or the use of expectorants and cardiac tonics. Ed.]

Patients seen in the earlier stages, even though already the subject of some degree of bronchitis and possibly venous torpor, may be considerably aided by general **massage** and **exercises** of the character known as setting-up exercises, now commonly practised in classes in the various gymnasia, but equally practical if a patient can be induced to employ them at home.

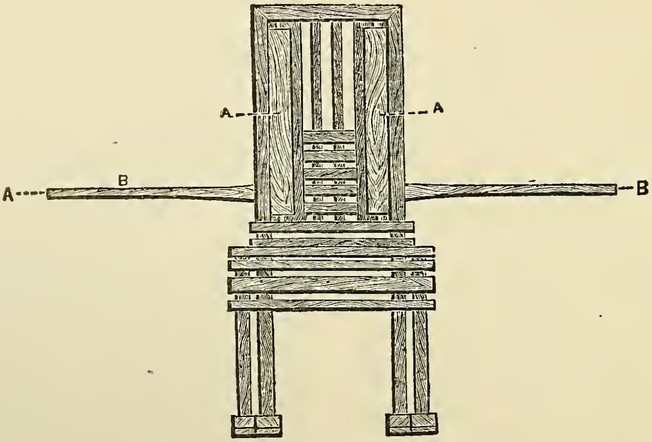


Fig. 1.—Rossbach chair, corset removed.

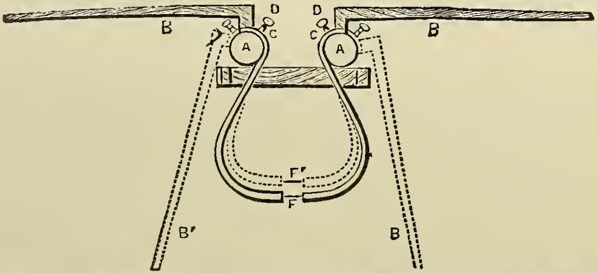


Fig. 2.—Rossbach chair, view from above, showing corset bandage (Illustrirte Monatsschrift f. aerztliche Polytechnik.)

When the venous circulation is defective, throwing extra work on the right heart, with congestion in the abdominal vessels, transient benefit may often be realized by tying off the limbs as a bloodless substitute for venesection. This is proving a useful means to influence favorably acute weakness of the right and left heart manifesting itself in pulmonary edema. The writer has confirmed by extensive animal experimentation the effectual action of this method of retaining the blood in the periphery. The heart grew smaller, both the arterial and venous blood-pressure dropped, etc., and patients with emphysema disturbances felt relieved as soon as their limbs were thus excluded from the general circulation. Tornay has reported similar benefit in congestion from cirrhosis of the liver, and Lilienstein has recently devised what he calls a "phlebostat" to accomplish this bloodless bloodletting. The writer commends this measure as a simple and harmless means to relieve extra strain on the venous heart. It can be applied with any simple **constricting band** or **tourniquet, to both arms and legs** at the same time, applying the constriction so as to arrest the venous circulation but without interfering with the arterial circulation. By this means it is possible to drain as much as a liter of arterial blood into the limbs and hold it there. After half an hour the constricting bands are gradually loosened. The procedure can be repeated two or three times a day. Von den Velden (Therap. Monats., July, 1912).

Spasmodic dyspnea, bronchitis, and cardiovascular phenomena are the three conditions which especially demand relief. The dyspnea and bronchitis almost invariably occur as associated factors, while the cardiovascular phenomena only present themselves in an urgent manner in the most advanced cases. It is to the former of these two, therefore, that our attention should be especially directed. For these it may be urged that absolute removal from all occupations, in which dust is a necessary accompaniment, is an absolute prerequisite. Change of climate is not possible to the great majority, therefore, all that remains is the use of general and rather vigorous **massage** and the practice of **gymnastic exercises** in the form of **calisthenics**.

In using the **mechanical measures** which have been employed to aid respiration in emphysema, the conditions to be dealt with are the lessened elasticity of the lung, the weakness of the respiratory muscles, and fixation of the thoracic framework. While a healthy man can exert an expiratory pressure of 100 to 150 mm. of mercury, in emphysema the figure is only 50 to 80 mm. The pressure exerted by the elasticity of a normal lung is about 18 mm. of mercury; hence the loss of this is not sufficient of itself to explain the great diminution of expiratory force, which must, therefore, be due to the other two factors. In the absence of any means of arresting or curing the degenerative changes in the lung tissue, treatment has been directed, first, to helping expiration by **pressure on the chest** wall during that phase: this may be applied with the hands, or by means of a special instrument, or by letting the patient breathe out into an artificially lowered atmospheric pressure. In these methods inspiration is not affected. Secondly, artificial respiration has been carried out by apparatus devised to help both the inspiratory and the expiratory process. Thirdly, exercises have been used to increase the power of the muscles used in each phase. Fourthly, an **elastic shirt or corset** has been worn to oppose inspiration while helping expiration. In reviewing these methods the author strongly recommends the last. He uses a **vest** composed **of** an **elastic tissue,** exerting pressure upon the lower part of the chest; by means of buckles the pressure can be varied. The vest is worn day and night. With this instrument the chest is kept in the expiratory position, in which the muscles of inspiration act at the best advantage. The obstruction to breathing in is found to have no drawbacks. On the contrary, it is in those cases in which weakness of the inspiratory muscles is marked that the best results are obtained, and the vest can be tightened as the muscles get stronger. The expiratory force and the expansion at each respiration can be shown by measurement to be improved, and the vital capacity may be increased from less than 100 up to 900 c.c. of air, the normal being about 500. The dyspnea is lessened and the patient enabled to return to work, if it be not of too severe a character. The treatment is unsuitable when there is almost complete fixation of the chest wall. Wolf (Wiener Klinik, April, 1905).

The writer gives **iodine** and **arsenic** and has the patient exercise in a **Waldenburg apparatus,** breathing in compressed air. In one of the cases described, the lungs have returned to normal size and the expiratory force has risen from 40 to 95, while the patient has gaied about 20 pounds in weight. De Renzi (Gaz. degli ospedali, xxviii, Nos. 30-36, 1907).

For the spasmodic dyspnea, the more urgent its character and the more akin to asthma, the greater will be the need of an **opiate** in some form. The acute attack having subsided, it will be advisable to use **belladonna** and the **iodides**, with **strychnine** used separately owing to its incompatibility with the iodides.

> Elasticity in the chest wall is the main factor to be combated in the treatment of emphysema. Of the operative measures which aim to restore this elasticity, **chondrotomy** is indicated before the condition has entailed atrophy of the muscles of respiration and severe disturbances in the circulation. (See below). **Potassium iodide** is still the best expectorant for bronchitis with emphysema. **Epinephrin** has a favorable influence in asthma, probably from the anemia it induces in the mucosa of the finer ramifications of the bronchi, thus reducing the resistance to expiration. The benefit from sweating procedures, **electric light baths,** is probably from the same mechanism. All measures are rational and useful which aid in strengthening the muscles of respiration and promoting expiration of residual air. Of special importance is the strengthening of the diaphragm. Minkowski (Therapie der Gegenwart, Feb., 1912).

Counterirritation, or **cupping,** during the acute phases should be resorted to, and in the intervals between the acute attacks, at which time only should the exercises be practised; effort should be made, through the medium of **iron, arsenic,** and **strychnine,** to improve the patient's nutrition.

Particular attention, at all times, should be given to the bowels, both with the idea of preventing tympanites, which mechanically interferes with respiration, and because the straining attendant upon constipation is liable to further damage the pulmonary structures.

> The respiratory passages should be kept in an aseptic condition. The writer recommends:—
>
> ℞. *Bismuth subnitrate,*
> *Boric acid*....āā gr. lxxv (5 Gm.).
> *Camphor, finely powdered* .... gr. cl (10 Gm.).
> *Cocaine hydrochloride* ..... gr. 3/10 (0.019 Gm.).
> *Menthol* .... gr. ¾ (0.048 Gm.).
>
> Mix thoroughly. Sig.: For a snuff.
>
> Before using the foregoing, the passages may be washed with a 3 per cent. solution of borax. The same solution, flavored with mentholated alcohol, may be used for the mouth and throat, or a good liquid dentifrice will serve.
>
> As to internal treatment by drugs, the writer prescribes:—
>
> ℞ *Sodium arsenate.* gr. ¾ (0.048 Gm.).
> *Potassium iodide.* gr. lxxv (5 Gm.).
> *Distilled water..* ℥x (300 c.c.).
>
> M. Sig.: Large tablespoonful ten minutes before meals. Continue for ten days, then intermit.
>
> For the ten days of intermission, order:—
>
> ℞ *Strychnine sulphate* .... gr. 9/20 (0.03 Gm.).
> *Distilled water.* ℥x (300 c.c.).
>
> M. Sig.: Dessertspoonful twice a day.
>
> All treatment of pulmonary emphysema is more or less palliative, as the condition is essentially chronic. Robin (Thérap. usuelle du praticien, 1911; N. Y. Med. Jour., Sept. 9, 1911).

Turpentine, terebene, cubebs, copaiba and such remedies of alleged value, where the expectoration is excessive, possess very little, if any, efficacy, at the same time having the disadvantage of greatly disturbing digestion. An occasional **blue mass pill** or a dose of **calomel** at bedtime, followed by a **saline** in the morning. In those who, for any reason, will not or can not exercise, the more or less continuous use of **fluidextract of cascara** may be employed, both for their effect on the bowels and indirectly for their effect in improving digestive secretions. In the later stages, when cardiovascular symptoms supervene, **venesection** may be necessary, and, indeed, is sometimes absolutely demanded to relieve overdistention of the right heart. Some one of the **digitalis** group, preferably the infusion or the tincture of digitalis may then be employed.

In emphysema and chronic fibrous pulmonary and pleural conditions **thiosinamine** diminishes dyspnea to some extent. Daily dosage of 0.06 to 0.10 Gm. (1 to 1½ grains) by injection or ingestion can be safely employed. It is contraindicated in tuberculosis. Rénon (Bull. de l'Acad. de Méd., April 25, 1911).

Surgical measures, particularly **Freund's chondrotomy** or **resection of costal cartilages** that are the seat of pathological changes which annul their elasticity and prevent the descent of the ribs, thus giving the chest the characteristic barrel-shape, are useful in some cases.

Freund's operation, resection of the cartilage of the first rib, is of unquestionable value in emphysema with rigid dilatation of the thorax; but it can have a good result when performed on one side alone. It is not particularly difficult in its technique, and is not too severe upon the patient; it should be recommended to resect the sympathetically affected cartilage of the first rib. The preferable time is the period of the appearance of dyspnea on moderate exertion, the latest time that of the appearance of dyspnea on very slight exertion; it is of value even when secondary insufficiency of the heart is present, but once in a while so advanced a case should be advised against the operation. Pässler and Seidel (Münch. med. Woch., Sept. 17, 1907).

Freund's operation is indicated where the pathological findings are as follows: the costal cartilages are of a dirty yellow color, in a state of fibrillation and cystic, showing also calcareous deposits which cause them to become increased in size; they are hardened, brittle, and devoid of their normal elasticity. When such changes are present, the proper excursion or motion of the corresponding ribs is interfered with. The cartilages of the second and third ribs of the right side are most frequently involved, but these changes may involve all the costal cartilages. The first cartilage, however, is rarely, and then usually the last, to be involved in this disease. With the degeneration of the cartilages and the accompanying rigidity of the ribs, the sternum is forced outward and contributes eventually to the formation of the rigid barrel-shaped thorax, which retains the lung in a continued state of distention. With the increase in the diameters of the chest, the normal function of the diaphragm is interfered with, and the muscle shows evidences of atrophy and fatty degeneration. By removing or resecting the offending cartilages, the proper functioning power of the chest may be restored; the ribs wlil be permitted to exercise their proper range of motion, and the proper expiratory efforts of the lungs will be facilitated.

The writer found that Freund's operation is of great benefit in emphysema with a rigid dilated condition of the thorax. A most convincing feature of this treatment is observed during operation; when the costal cartilage is resected the rib recedes immediately, at times below the level of the sternum. The ribs move so freely that the finger tip is distinctly squeezed when inserted between the sternum and rib. The lung visibly contracts. Relief may be afforded by operating upon one side. The operation is not dangerous, and is not followed by shock. Cardiac insufficiency, asthma, chronic bronchitis, and albuminuria are not necessarily contraindications of the operation. The best results are obtained, however, when the operation is undertaken before complications have arisen. Goodman and Wachsmann (Med. Rec., May 16, 1908).

It cannot be urged too strongly that routine physical examinations should be made of all patients presenting themselves for treatment, irrespective of the condition. It will often be possible to detect those morbid states which invite the development of emphysema and to recognize early stages of that disease at a time when it may be possible to be of distinct service.

W. Egbert Robertson,
Philadelphia.

EMPHYSEMA, SUBCUTANEOUS.—Besides the pulmonary emphysema described above, there are others in which the spaces of connective tissue under the skin become infiltrated with air, viz., *cutaneous* or *subcutaneous emphysema.* There are besides, the artificial or false forms in which gases of microbic origin are the pathogenic agents, viz., *septic or gangrenous emphysema.* (See Gangrene.) *Traumatic emphysema* and *surgical emphysema* are additional types due, as their names indicate, to traumatism or injuries and to surgical procedures, which were referred to under the preceding heading.

SYMPTOMS.—Subcutaneous emphysema—the only type here considered—appears as an ill-defined edematous swelling which pits under pressure, imparting to the finger a fine crackling sensation. After rupture of the lung it rarely occurs unless there is pneumothorax. The emphysema first appears at the root of the neck about the trachea and great vessels, reaching there along the bronchi, trachea, and vessels from the pleura. It also infiltrates the tissues about any wound in the parietal pleura.

After wounds of the lung there is often an infiltration of air about the external wound, and this is especially liable to occur if the wound is small or roughly sutured so that the air may, by the variations of intrathoracic pressure, be forced into the deeper tissues, but not through the skin.

TREATMENT.—Circumscribed subcutaneous emphysema is rarely a matter of any moment; it is usually slight in extent and quickly absorbed. It rarely ends in suppuration. But if the laceration in the lung acts as a valve, pumping air into the lung with each inspiration and allowing none to escape with expiration, the emphysema may spread over all the thorax, even over the whole body, in which case the danger is from suffocation.

> Half an hour after being run over by a wagon, a robust, 8-year-old boy was found to be suffering from emphysema, extending over the whole body except the palms and soles. Penis and scrotum were so puffed up as to resemble oblong rubber balls, and an attempt to hold the eyelids open with adhesive straps proved unavailing because of the tense state of the skin. The tissues under the scalp were also involved, crackling being distinctly perceived. The skin of the whole body was tense and pale. There were slight contusions on the elbow and chest. Respiration was labored. Palpation disclosed fractures of the sternum and second right rib. Three hours later the emphysema had so increased as materially to interfere with respiration; skin stretched almost to the limit of its elasticity; increasing cyanosis. On incising the chest the effect was instantaneous, as if a tense rubber ball had been pricked, and breathing immediately became deeper and slower. Two rubber drainage-tubes were inserted and left in for five days. C. G. Molin (Brooklyn Med. Jour., Oct., 1897).
>
> A child of 8 years with Pott's disease began to cry out, became excited, and complained of severe headache. This was followed by stiffness of the neck, photophobia and obstinate constipation, and the diagnosis of tuberculous meningitis was made. Suddenly respiration became labored, Cheyne-Stokes, the eyelids and cheeks swelled up, and the eyeballs protruded. This edema gave a fine crepitation and was evidently subcutaneous emphysema. Soon both sides of the neck and the upper part of the chest were involved and the patient was comatose. She rallied somewhat for a time, but the emphysema progressed, and death took place aften ten days. At the *post mortem* there was found an intrapulmonary rupture of a sub-

pleural tubercle, without perforation of the pleura. The air penetrated the interlobular tissue, and thence reached the mediastinum, neck, and face. P. Guillaume-Louis (Arch. gén. de méd., Aug. 18, 1903).

The emphysema in the writer's case occurred in the face during the first stage of labor. This swelling increased and was accompanied by cyanosis during the pains. The crackling sensation of subcutaneous emphysema was found present over the swollen area, extending over the neck and right side of the face; the right palpebral fissure was reduced to a slit. Forceps were applied and the patient was delivered of a living child. Within about seven hours the emphysema was found present over an area including both sides of the neck, both sides of the face up to the orbital ridges, the whole of the right side of the thorax limited by the costal margin below, the spine behind and the sternum in front; the right upper arm to the extent of a third, and the left shoulder. Apart from some pain in the chest and at the back of the neck, of which complaint was made, the patient appeared to be little the worse. She made a good recovery, the whole of the swelling having disappeared at the end of eight days. Stock (Lancet, March 16, 1912).

The treatment is **multiple incisions.** At the same time the intrathoracic pressure must be relieved by **paracentesis** or **drainage.**

Emphysema following exploratory puncture of the chest has rarely been reported. Three cases are related.

In puncturing the chest one must not forget the possible proximity of firm and unyielding lung tissue to the chest wall, and the author thinks the operation is too often undertaken with disregard of the element of danger, especially in children. When a small collection of fluid overlies a more or less consolidated lung diagnosis by percussion and auscultation is often unsatisfactory, and **puncture** becomes imperative, **but the lung must be avoided** unless one is searching for an intrapulmonary collection of fluid. Gittings (Archives of Pediatrics, Jan., 1908).

Case of a primipara, aged 33, who, after a prolonged labor in which delivery was affected by axistraction forceps, gave birth to a male child on Sept. 22, 1910. Although the heart was working well, artificial respiration had to be employed for about twenty minutes as the infant at first refused to breathe, and a large quantity of liquor amnii was expressed from the mouth and nose. The following day acute edema developed over the head, thorax and scrotum. The bowels and urine were normal. On September 26th, the child, which had been crying lustily for the last twenty-four hours, suddenly became silent. The edema was then being rapidly replaced by a subcutaneous emphysema over the front and back of the head and thorax. The child could swallow well, but had complete aphonia. The breathing was slightly stridulous. There was no cough.

Hot fomentations were applied to the **neck,** the nostril and nasopharynx were sprayed with **normal saline solution,** and 3 ♏ (0.18 c.c.) doses of wine of **ipecacuanha** were given every two hours. At midnight the emphysema had increased, and there was considerable dyspnea. Râles and rhonchi were heard over both lungs, the respirations were 48, and the pulse was feeble. The infant was listless and showed no desire for food. **Hot fomentations** were then applied to the **chest and back** and 20 ♏ (1.25 c.c.) of **brandy** were given every hour, together with wine of **ipecacuanha** and **syrup of tolu** and **squills.** The following day, September 29, the child was better generally, and took its food well. The emphysema was less on October 1, the child could cry loudly and the emphysema had almost gone. Recovery followed. (Brit. Jour. of Children's Dis., Feb., 1911). S.

EMPYEMA. See PLEURISY.

ENCEPHALITIS. See MENINGES AND BRAIN, DISEASES OF.

ENDOCARDIUM AND VALVES, DISEASES OF.—Under this head will be considered the various inflammatory disorders of the endocardium and of the cardiac valves which form part of the endocardium.

ENDOCARDITIS.—DEFINITION.—Inflammation of the membrane lining the cavities of the heart. The process may be acute or chronic. The acute form is variously described as "simple," "benign," or "verrucose," and "ulcerative," "septic," or "malignant," according to the mildness or severity of the disease; but between these two forms there is in reality no dividing line. The disease attacks mainly the valves of the heart.

ACUTE ENDOCARDITIS.

SYMPTOMS.—The onset of acute endocarditis is insidious. There may be no symptoms which call especial attention to the organ affected. There may be a slight rise of temperature and some quickening, and possibly some irregularity, of the pulse. In the benign form there may be no evidence of the disease until two or three months after it has run its course, when impairment of the valves is detected. In some cases there is precordial pain, or, if the patient is a child, there may be epigastric distress, with vomiting. The pulse is of low tension, and the patient may be restless and anxious, and may prefer a somewhat recumbent to a horizontal position. Examination of the heart will disclose in most cases a murmur, usually of a blowing character, and usually systolic in time. It may accompany or replace the normal sound. Before there is an actual murmur, it may be possible to detect an impurity and prolongation of the first sound of the heart, indicating involvement of the mitral valve. Even in the malignant form the symptoms may be masked by those of the original disease. In the severer cases sometimes there is a true chill or a succession of chills, and the fever may be either typhoidal or intermittent or remittent in its character. The patient gives evidence of great prostration. The pulse is rapid and irregular; the body bathed in profuse perspiration; the spleen enlarged and tender. There may be a rose-colored eruption upon the body; more often petechiæ are seen. The number of white corpuscles in the blood is greatly increased.

In some cases, even the worst, careful and repeated examination by competent observers may detect no cardiac murmur whatever.

The simple form may give rise to embolism in different parts of the body, and may also be complicated by pleurisy or pneumonia. The malignant form is still more apt to give rise to emboli than is the simple form, and also frequently distributes infection. In fact, scarcely any tissue is exempt from these dangers. Thus, there may be embolism of the brachial, femoral, or external iliac arteries, or of the capillaries of the skin. There may be infarctions in the spleen, causing a swelling and tenderness of that organ; in the kidneys, giving rise to renal hemorrhage; in the brain, with resulting paralysis or softening; in the intestines, with bloody stools. The retina, conjunctiva, gums, parotid gland, and stomach may be affected. In some cases there is acute jaundice, with symptoms simulating acute yellow atrophy of the liver, and, as just stated, these lesions are not merely mechanical, but infectious, and apt to give rise to suppuration.

When acute endocarditis is due to recurrence of inflammation in a valve previously fibrotic, abscesses are unusual.

The duration of the disease in the milder cases is usually from two to six weeks, perhaps in most instances about four weeks. The malignant cases may reach a fatal termination in one or two days, or, again, they may be prolonged for several months or a year, and then prove fatal. Some cases of simple endocarditis are not suspected during their course nor betrayed by sequelæ; thus, minute vegetations may be found, *post mortem,* upon the valves of patients who die of consumption or of carcinoma, which have been of no importance whatever. The great harm that simple endocarditis does the patient is not immediate, but consists in laying a foundation for ultimate changes in the valves, which impair the functional integrity of the heart.

As seen in practice, infective or ulcerative endocarditis does not always correspond with the description in books. In a series of cases witnessed by the writer, the most prominent symptom was oscillation of the temperature, with rigor or evidence of infarction. Other symptoms were petechiæ of the extremities, vomiting, ashy discoloration of the skin, and heart murmurs. A murmur is not always present; when present it may be loud and persistent, if added to pre-existing chronic valvular lesion, or it may be soft, and finally become inaudible. The deposits upon the heart valves are invariably on the side over which the blood passes in its onward flow, and that the vegetations are soft and spongy. As they do not prevent closure of the valves, an absence of cardiac murmur is not necessarily strange. The vomiting and retching, which may follow a succession of rigors, without any discoverable gastric, hepatic, or cerebral change, may be considered as analogous to the vomiting of uremia, or of cholemia. The septic cerebral and typhoid types of symptoms are probably due to the presence of a toxine in the circulation. N. Tirard (Practitioner, Nov., 1908).

DIAGNOSIS.—The first question to settle with regard to diagnosis is whether any endocarditis exists at all, and, secondly, whether the form is simple or malignant. There may be no objective cardiac signs distinctive of the disease. Usually, however, there is a systolic apical murmur, and the heart is enlarged, with a more widely diffused impulse than normal, and an excited—though feeble—action.

It should be borne in mind that many of the diseases with which acute endocarditis is etiologically associated give rise to functional cardiac murmurs, so that the mere discovery of an abnormal sound over the heart does not establish the diagnosis.

Typhoid fever is more gradual in its onset and has a small number of white blood-corpuscles contrasted with the leucocytosis of endocarditis, and an infrequent pulse. Moreover, the Widal reaction is distinctive of typhoid, as would also be the discovery of typhoid bacilli in the blood or the stools. Typhoid may give rise to infarctions, and to inflammation of the parotid, but not often.

Acute tuberculosis has its hectic fever, rapid wasting, possible pulmonary signs, sometimes tubercle bacilli, and, as a rule, no objective cardiac symptoms.

Malarial fever may be recognized by the discovery of the characteristic organisms in the blood.

Septicemia and **pyemia** have symptoms identical with those seen in certain forms of malignant endocarditis, which disease has, indeed, been called an arterial pyemia. In some acute cases there is possibility of confusion with typhus fever, cerebrospinal meningitis, abscess of the liver, and hemorrhagic small-pox.

In **severe infectious diseases**, unless there be signs of obstruction of a valve, it may be impossible to determine whether there be endocarditis or a myocarditis due to toxins, rendering the wall flabby and the mitral valve relatively incompetent.

ETIOLOGY.—Endocarditis is an infectious disease, and almost always secondary to some other. It is most frequently an expression of rheumatism. It may follow tonsillitis, pleurisy, chorea, measles, small-pox, and any acute infectious disease, particularly scarlet fever. Pneumonia, influenza, erysipelas, gonorrhea, pericarditis, and meningitis may present this complication, as may also, in rare instances, typhoid fever, tuberculosis, and diphtheria.

> Case of gonorrheal urethritis which developed endocarditis. The gonorrhea had been contracted shortly before, and it became necessary to catheterize this patient a few times immediately following an operation. The case suggests that the passage of the catheter over the inflamed mucous membrane of the urethra had opened up the atrium for the passage of the bacteria, or dislodged a small thrombus which was swept into the blood-stream. Rothrock (St. Paul Med. Jour., Nov., 1911).
>
> This complication is rare, both in children and adults, in typhoid fever. The only definite sign of its presence is embolism, and this is itself an infrequent accompaniment. Endocarditis in typhoid is generally due to secondary infection from a focus of suppuration in the skin. Previous rheumatic or tuberculous valvular disease appears to be, as a rule, a necessary predisposing factor. Savy and Gardère (Revue de méd., Sept., 1912).

Osteomyelitis, puerperal fever (as well as other vaginal or uterine affections), empyema, bronchiectasis, external wounds, and any form of septicemia may occasion endocarditis. Cancer, gout, diabetes, and Bright's disease may give rise to it.

> So many cases of acute endocarditis were witnessed by the writer in Vienna in the last few months that he wonders whether it is possible for this disease to occur in epidemic form. The patients were all between the ages of 6 and 18 and the clinical course was alike in all, beginning with moderate fever without angina or joint symptoms; only later there were pains in one or both ankles in a few cases. Multiple articular rheumatism did not develop in any case, but in the second week there was tachycardia, accompanied later by palpitations, pains in the apex region, rapid breathing and cyanosis, with a dry cough, especially at night. Herz (Wiener klin. Woch., March 23, 1911).

Almost invariably some form of bacteria is found in the lesions, but there does not seem to be any bacterium peculiar to the disease. In rheumatic cases there would seem to be a specific diplococcus, but in both the simple and malignant forms the pyogenic micro-organisms are those most often encountered, namely, streptococci, staphylococci, pneumococci, and gonococci.

> In 2 young women who had been making attempts to procure abortion, there was in each a sudden attack of severe illness, miscarriage occurred, and death rapidly followed on a profound toxemia. These two deaths resulted from infective endocarditis, the fatal issue being possibly hastened in the second case by uremic conditions fol-

lowed on the widespread changes in the kidneys. It seems justifiable to conclude that the occurrence of miscarriage was the inevitable result of the infection. Norton (Lancet, Jan. 15, 1910).

Case of meningococcus endocarditis with septicemia. The meningococcus, in spite of its affinity for the meninges, may at times become lodged on the endocardium, with the production of an acute vegetative endocarditis. In this respect it resembles most of the other pathogenic bacteria, which, while showing a predilection for some particular organ or tissue, may occasionally produce serious lesions in other parts of the body. The symptoms and pathological anatomy of meningococcus endocarditis correspond to those which characterize malignant endocarditis of streptococcus or pneumococcus origin. It may or may not be associated with cerebrospinal meningitis. The portal of entry for the organism in meningococcus endocarditis is probably the upper respiratory tract. Cecil and Soper (Archives of Intern. Med., July, 1911).

Examination of 100 cases to see whether by clinical and post-mortem examination there is any confirmation of the view that there is an infective endocarditis. In 58 cases of the 100 there were old cardiac lesions, as shown by the necropsy. Of the remaining 42 there was doubt in 8 cases. In 27 cases there was an infective focus from which it might reasonably be supposed that the septicemia arose. Of these 27 cases there was a rheumatic history in 7 and there were old cardiac lesions in 10. Of the remaining 73 there was a rheumatic history in 52 cases and old cardiac lesions in 48, and in 9 of the remainder it was doubtful as regards old cardiac lesions. These figures bring out one point strongly: In the 27 cases in which an infective focus was found, and which no one could reasonably call rheumatic in origin, there is a history of rheumatism in 7 out of 27—*i.e.*, 25.9 per cent.—while in the 73 in which no infective focus was found there was a rheumatic history in 52 cases—*i.e.*, 71.2 per cent. Infective endocarditis, supervening in the course of some particular disease as rheumatism or pneumonia, may be regarded as directly produced by the causes which have excited the original disease. Venning (Lancet, June 17, 1911).

The relation of hypertrophies and of infected tonsils to endocarditis is not regarded as such a definite one as is held by some. Among 2000 tonsillectomy cases at the Memorial Hospital at Worcester, heart lesions were found to be extremely rare. Not all heart murmurs mean endocarditis. While experimental and clinical evidence show the mouth and throat to be portals of entry of infectious agents, which later may invade the heart, it does not follow that the tonsils are the sole portal of such entry nor, indeed, that they are an essential agent in the infection. A. C. Getchell (Annals of Otal., Rhinol. and Laryn., Sept., 1911).

Before birth the right side of the heart is almost exclusively affected; after birth, the left. Early adult life furnishes a majority of the cases, and, according to the latest statistics, men are somewhat more liable to the disease than women.

Several cases have been ascribed to traumatism.

Case of a musician, aged 35, who, returning from a playing engagement in the early morning hours, was attacked by foot-pads. He escaped by running, though rather heavily loaded with his music and instrument, and reached home utterly spent and exhausted. For half an hour he had to stand up and struggle for breath. The sense of suffocation, however, gradually left him and was followed by a depressing palpitation, lasting until the next day. Two or three months later it returned and has been intermittingly troubling him ever since. Examination showed a presystolic thrill in the apex region, a loud churning presystolic mitral murmur, accentuation of the second pulmonic sound and also, on a later examination, a doubling of the second sound at the base of the heart. Before the episode mentioned he was perfectly sound and well so far as known and his history was negative as regards disease. While admitting the difficulty of proving a given case of heart disease to be the result of trauma, the writer believes the endocardial lesion was the direct result of the violent strain and exertion. D. Riesman (Jour. Amer. Med. Assoc., Sept. 30, 1911).

PATHOLOGY.—It has already been said that clinically there is no dividing line between the simple and malignant forms of endocarditis. This is also true pathologically. The simplest lesions consist of minute warty vegetations, varying from 1 to 4 mm. in diameter, seated upon the valves. These are composed of fibrin, leucocytes, blood-platelets, and micro-organisms. Sometimes the vegetations are so abundant as to obstruct the valvular orifice. Even in the simple form (endocarditis verrucosa) there is more or less ulceration of the valvular endocardium. In the malignant form (endocarditis ulcerosa vel diphtheritica) necrosis is more extensive. The valve may be so thinned as to give way under the pressure of the blood, thus producing a valvular aneurism, or actual perforation of the valve. A portion of the valve may be broken off, or some of the chordæ tendineæ may be ruptured.

Case in which rupture of the chordæ tendineæ followed an attack of acute endocarditis during which the chordæ became enlarged and softened, pathological changes which favored their rupture. Fifty cases of ruptured chordæ were found in literature, divided into 5 classes. In 7 cases the rupture was due to severe traumata, such as fractured ribs from violent compression, falls from a considerable height, stab wounds, gunshot wounds, and the kick of a horse. Five cases were due to efforts, such as straining, lifting, excessive fatigue, and severe cough in which no endocardial lesions were disclosed by the autopsy. In 9 cases the rupture was due to or preceded by strain, without endocardial or myocardial lesions. In 19 cases, in which no endocardial lesion was found, there was no history of strain or trauma. The writer's case had a presystolic murmur without mitral stenosis. L. F. Frissell (Med. Record, April 20, 1912).

The vegetations are situated mainly on that surface of the valve which is opposed to the blood-current. Thus, the lower surface of the aortic valves and the upper surface of the mitral valves are chiefly affected.

As the result of a study of 287 cases of endocarditis, both acute and chronic, which came to the autopsy table, the author found that myocardial disease is present in greater or less degree in practically all cases. In most instances the myocardial change is not determined by and is not the direct result of the endocarditis, but is caused independently by the same, affiliated, or entirely independent conditions. The form most frequently seen in chronic or late acute cases is fatty degeneration, a lesion which differs in no material histochemical respect from that involving voluntary muscle. From analogy, it seems that this degeneration in most instances succeeds a primary parenchymatous alteration. As a sequence to fatty degeneration, fibrous replacement and probably brown atrophy frequently appear. Treatment in endocarditis is mostly based on recognition of the dominance of the muscle factor, and in nearly all, except possibly syphilitic, cases it is without effect on the valvular change. Harlow Brooks (Amer. Jour. Med. Sci., Dec., 1911).

To ascertain how an infection takes place, whether by direct inoculation or by septic emboli and thrombi in the vessels of the leaflets the writer conducted an investigation. His results agreed with those of Ribbert, Orth and others, that the cocci were deposited upon the leaflets from the circulating blood and not within them as emboli. The possibility of an embolic origin of endocarditis in man is not denied, yet none of the experiments furnishes any basis for such a belief. Lissauer (Zentralbl. f. allg. Path. u. path. Anat., March 15, 1912).

Exceptionally the heart wall suffers, sometimes leading to cardiac aneurism, or perforation of the ventricular septum, or perforation into the pericardium.

The associated lesions peculiar to endocarditis are mainly caused by emboli, and, yet, it is a surprising fact that sometimes, even when the valvular lesions are decidedly ulcerative, no evidence of embolism may be found *post mortem.*

The term *"endocarditis lenta"* is applied by the writer to an infection localized in the endocardium, the germs sallying forth thence occasionally into the blood. The germ in question he had isolated ten years ago, entitling it the *Streptococcus mitior seu viridans;* it is not very virulent but induces necrosis in parts of the endocardium, leading to wart-like efflorescences and causing a clinical picture distinguished by the insidious onset, the vague slight pains in the joints and groups of muscles, with palpitations and dyspnea and a dry cough, the latter causing the suspicion of a lung rather than of a valvular affection, especially if the patients are pale and anemic. In the cases in his experience there were evidences of mitral endocarditis. At first there were no audible murmurs in some cases, but the persistent fever suggested the true diagnosis. Schottmüller (Münch. med. Woch., March 29, 1910).

Schottmüller's *endocarditis lenta,* caused by the *S. viridans,* has a sufficiently distinctive picture to deserve recognition as a separate clinical entity. While cases of chronic endocarditis may also be due to the *B. influenzæ, S. pyogenes,* or pneumococcus, such cases should be distinguished from those due to *S. viridans,* just as epidemic cerebrospinal meningitis, for example, is distinguished from meningitis due to the *B. tuberculosis, B. influenzæ* or *S. pyogenes.* The coccus present in the cases cited by the writer correspond culturally to the organism described by Schottmüller as the *S. viridans.* No essential cultural differences have been noted between the *S. viridans* and *M. rheumaticus.* Major (Bull. Johns Hopkins Hosp., Nov., 1912).

Embolism affects the spleen and kidneys most frequently, and also many other organs, as above enumerated. If the right side of the heart is affected, there may be multiple pulmonary abscesses.

A study of the lesions produced experimentally by the injection of sparteine sulphate followed by the injection of adrenalin chloride showed that drugs introduced into the circulation produce proliferative changes in the endocardium. The most marked changes were in the endocardium covering the papillary muscles, though they occurred elsewhere, even in the auricles. The valves were free in most cases. The endocardial lesions were practically confined to the animals that received sparteine sulphate and adrenalin chloride. Uranium nitrate, potassium bichromate, and arsenic in various forms caused constant renal changes, but had no effect upon the endocardium. Christian and Walker (Proc. Amer. Soc. Adv. of Clin., 1910).

PROGNOSIS.—First, it is possible for very slightly developed cases of simple acute endocarditis to recover without any real damage. The great danger from the non-ulcerative form, besides embolism, is the setting up of a chronic fibroid deterioration of the valve, ultimately impairing its efficiency.

In rheumatic endocarditis the presence of rheumatic nodules over the bony prominences of the joints, in children and young adults, indicates that the attack is severe.

The malignant forms are almost invariably fatal. Cases in which the acute process has been kindled upon the remains of a former valvular inflammation are somewhat more hopeful.

TREATMENT. — First, **prophylaxis**: Persons with rheumatic tendencies should be guarded against attacks by **cold sponging, woolen underclothing,** and **avoidance of cold and wet.** The tonsils, being a frequent gate of entrance for rheumatic and other infections, should be put in good order.

[When in a case of acute endocarditis examination shows any morbid condition of the tonsils, pure **tincture of iodine** should be applied to them with a camel's hair pencil, daily. Ed.]

> Rheumatism and endocarditis are in great measure results of diseased or **infected tonsils** which should be **removed.** Even as a prophylactic measure such tonsils are better out than in. B. R. Shurly (Detroit Med. Jour., Feb., 1911).

Patients who simultaneously suffer from rheumatism should be kept as quiet as possible. The salicylates do not seem to lessen the liability of such patients to endocarditis. It may be that the administration of **alkalies** in sufficient amounts to keep the urine neutral is of some advantage.

> The use of **salicylates** and alkalies for the suppression of the rheumatic poisons is the best means by which the effects of that poison on the cardiac tissue can be overcome. The application of **leeches** or of **ice** or of a succession of **small blisters** or of **iodine over the precordium** are all measures of relief useful in many instances. Choice must be made of the one most suitable to the requirements of the case on hand. In many instances the pain and restlessness in the earlier stages of the illness are so intense as to necessitate the use of **morphine.** On the first evidence of cardiac failure **strychnine** ought to be given hypodermically and should be combined with **digitalin,** should the pulse, despite strychnine, remain small, quick, and irregular. If dyspnea becomes urgent, and especially when it is accompanied by cyanosis, recourse should be had to inhalations of **oxygen.** In malignant cases the same line of treatment is indicated, but, in these, **quinine** sometimes seems to be a more effective remedy than sodium salicylate. When resorted to it ought to be given in full doses. When the organism upon which the disease depends can be determined, the patient ought not to be denied the chance which is afforded by inoculation with a suitable vaccine. Rankin (Practitioner, July, 1911).

In the various children's diseases the only way in which we can protect the patients from cardiac complications is by insuring **bodily quiet** and good ventilation and avoiding exposure to cold.

In gonorrhea such internal antiseptics as **salol** and **urotropin** are advisable.

Second, when the disease has actually developed, an **ice-bag** wrapped in flannel may be kept over the heart if not disagreeable or depressing to the patient. Or, instead of this, a thin **layer of cotton-wool** may be applied. Violent counterirritants are not indicated. If the heart's action is excited, **bromide of sodium** may be administered. Still more efficient, and in case of cardiac distress indispensable, is **morphine,** used in carefully regulated amounts.

> In case of a septicopyemic affection, besides the local measures, the writer obtained good results with quinine, giving 0.3 or 0.5 Gm. (5 to 7½ grains) **quinine hydrochlorate** several times a day to act on the bacteria in the blood. It may have to be kept up for weeks, adding **iron** in case of anemia. This treatment acts on the deposits of bacteria in the endocardium, but it acts very slowly, so that the lack of evidences of improve-

ment in the first few weeks should not deter from continuing the treatment. If not tolerated by the mouth, the quinine can be given by the rectum or, possibly, subcutaneously. G. Hoppe-Seyler (Deut. med. Woch., Bd. xxxiii, Nu. 4, 1907).

If there is stagnation of pulmonary circulation, **ammonium carbonate** is indicated. **Aromatic spirit of ammonia** is a good stimulant. If rheumatism is connected with it, **chloride of gold,** ⅛ to ¼ grain (0.008 to 0.016 Gm.) three times a day, is a fine remedy in this condition; so is fld. extr. **cimicifuga,** 15 to 20 drops three or four times a day. Its antispasmodic, diuretic, and diaphoretic action is valuable and efficient; small doses increase secretion; full doses increase the force of the heart and slow the rate. Cimicifuga is a valuable remedy in endocarditis and other heart troule. **Ammonia** is a good stimulant, but **whisky,** or **brandy,** is the best general stimulant we have. **Sparteine sulphate,** ⅛ to ¼ grain (0.08 to 0.016 Gm.) is a good stimulant and tonic. These two last, used hypodermically, slow and strengthen the heart beat and increase the cutaneous and venous circulation. The author has used **adonis vernalis** successfully in combating "heart-failure," pain, and dyspnea—tincture, 10 drops; **adonidin,** ⅛ to ¼ grain (0.016 Gm.) every three or four hours. E. C. Rothrock (Wisc. Med. Recorder, June, 1908).

Where there is marked danger of heart paralysis from acute dilatation nothing seems to be better than **strophanthin,** in doses of ½ to 1 milligram (1/120 to 1/65 grain) given directly into a vein. The action is very rapid, but unfortunately does not persist very long; so that it must be repeated, or other remedies must also be given. The drug is not so dangerous as some authors would have it, and as much as 1½ milligrams ((1/40 grain) daily have been given on two successive days, and 8.5 milligrams (⅛ grain) altogether in eight days. The cumulative action is very slight. Within a few minutes the pulse will fall in frequency, will become more forcible, and the dyspnea and cyanosis will disappear. The drug is generally regarded the last resort in cases of extreme cardiac weakness, though it may fail when **camphor** will still revive the heart. Where a more lasting action is desired, subcutaneous doses of **digitalone** or **digitalin-Nativelle** are in place. The latter resembles strophanthin very closely, but acts more slowly, while the action of the former is more prolonged. The technique of intravenous injection is very simple. It is better, however, first to introduce the needle without the syringe into the vein, so that none of the strophanthin solution will be deposited into the subcutaeous tissue. O. Hornung (Münch. med. Woch., Sept. 26, 1908).

Of great importance in these cases is **absolute bodily quiet,** and this should be maintained for at least four to six weeks. In case the heart begins to fail, recourse must be had to **digitalis, strophanthus, alcohol, ammonia,** and other cardiac stimulants, but in many cases their use will prove unavailing. Sometimes when the attack has been long continued, **arsenic** has been found beneficial.

In 2 cases of malignant endocarditis treated by the writer in which blood cultures showed the presence of streptococcus viridans, an organism which produces a subacute but extremely fatal form, he obtained recovery in one case by injecting intravenously **salvarsan.** He has tried a great variety of other methods of treatment in such cases without success. Lorey (Münch. med. Woch., April 30, 1912).

James Mackenzie is inclined to believe that in rheumatic endocarditis the **salicylates** may do good. He says that their employment is so frequently of use that it should always be tried, even pushing it at times. Lee states that large amounts of **salicylate of sodium** may be safely given, provided the bowels are kept open and the urine is kept alkaline with

bicarbonate of sodium, and provided, also, that the salicylate is temporarily suspended if unpleasant symptoms are produced.

To promote sufficient refreshing sleep, moderate doses of **bromide** may be found useful, but if not, other drugs should be used. The writer prefers among the various hypnotics **chloralamide** or trional, but if these do not suffice, **chloral** or **morphine.** The former is reliable, but its depressant effects must be considered, and he would give it only in the excited sthenic heart of rheumatic endocarditis; in the myocardial involvement, especially of pneumonia and diphtheria, he would not employ it. Morphine is reliable and safer. F. S. Meara (Jour. Amer. Med. Assoc., Feb. 3, 1912).

Specific sera and vaccines have also been used successfully.

The prognosis of pneumococcal endocarditis would appear to be exceedingly unfavorable, and the treatment by **vaccine** seems amply justified.

The only fully recovered case of acute endocarditis treated in this manner which the writer could find was one published by Barr, Blair Bell and Douglas in the Lancet, vol. i., p. 499, 1907. This case was streptococcal in origin, and also ended in recovery. A. F. R. Conder (Practitioner, Aug., 1909).

The writer urges the importance of using **vaccines** early, before the patient is so saturated with toxins as to be unable to react satisfactorily, and not to wait until all other measures have been tried and have failed. When it is realized by the profession generally, that there is just as much urgency in using vaccines as there is in the employment of antitoxins, more uniformly successful results will be obtained. J. R. Collins (Practitioner, Aug., 1909).

Various antistreptococcal serums, especially the so-called polyvalent variety, have been tried, but in view of the various micro-organisms, not to mention the many strains of streptococci, which may be responsible for the disease, it is rather hard to select the proper serum. The **vaccine** treatment would seem to afford a better chance of success, but when one considers how difficult it must be for the protective substances, even if formed, to reach the micro-organisms deeply seated in the affected valve through the very imperfect and slender channels through which the blood-supply reaches the valve, the chances of success do not seem very promising, and the vaccine treatment will in no way lessen the dangers of embolism. Moreover, in acute generalized infections, the vaccine treatment is not so hopeful as in the case of focal lesions. One case of recovery attributed to the vaccine treatment has been recorded. Broadbent (Practitioner, July, 1910).

Case of streptococcal endocarditis from a tooth abscess in a young married woman who had a congenital lesion of the endocardium. Ulceration of the mural endocardium caused innumerable infarcts in the lungs and a few in other tissues. Recovery occurred under treatment with **autogenous vaccines** and **autogenous serum.** In the early stages the pulmonary infarcts produced a picture closely simulating acute pleuritis of tuberculous origin. The use of the vaccine seemed to turn the tide of events in her favor, but alone was not successful, as immune serum was prepared from her organism by inoculation into a horse, and this, in addition to the vaccines, brought about the recovery. The fact of the valves remaining healthy doubtless facilitated complete recovery. H. Hemsted (Lancet, Jan. 4, 1913).

CHRONIC ENDOCARDITIS.

Chronic endocarditis may develop in a previously healthy valve. It is more often a sequela to acute endocarditis.

SYMPTOMS.—The symptoms are those of valvular disease of the heart, and are discussed under the next general head.

In the diagnosis of chronic endocarditis, it is important to adopt routine in the examination of the case in order not to overlook the condition present. The following order was adopted: mitral incompetency, mitral stenosis and aortic regurgitation. True organic mitral regurgitation conforms to the following picture: 1, Soft, blowing, systolic murmur, best heard at apex, but transmitted to axilla and to angle of left scapula; 2, accentuated pulmonic second sound; 3, enlargement of the heart—apex displaced downward and to the left, so that inspection and auscultation afford the greatest information in this condition. In mitral stenosis the chief clinical findings are (1) a presystolic thrill, rough, grating, felt in fourth or fifth interspace inside nipple line, ending in (2) a sudden, snappy shock, synchronous with ventricular systole; (3) a rough presystolic murmur heard in and usually limited to the area of thrill, ending in (4) a loud, snappy first sound at the apex; (5) accentuation of second sound in pulmonary area. Aortic incompetency presents the following group of signs: 1, The greatly displaced apex beat; 2, a long-drawn diastolic murmur heard at the base of the heart and best in the aortic area; 3, pulsating vessels in the neck, and 4, the water-hammer pulse of Corrigan. Rowntree (Jour. Med. Soc. of N. J., Feb., 1908).

In a series of 14 cases the disease manifested itself clinically over varying periods of time. In one patient, the symptoms began two years before the real condition was recognized. One case began fourteen months before a definite diagnosis was made. Another patient probably suffered from the disease for more than two years, and in the earlier part of the illness the diagnosis of typhoid was made for a condition which was, in all probability, infectious endocarditis, the diagnosis having been based on the fact that there was fever and splenic enlargement. No rose spots were found; there was no diarrhea, and the Widal reaction was negative throughout.

The infectious organisms found in the writer's 14 cases were as follows: The pneumococcus, 11 cases; streptococcus, 3 cases. The organisms obtained in the 11 patients suffering from pneumococcemia had many of the morphologic characteristics of streptococci. Study of the organisms in culture and in animals proved that they were the pneumococcus. In one patient of this series the infectious endocarditis followed pneumonia. Tonsillitis had occurred in 2 cases. In the other patients the source of infection could not be learned. There can be no doubt whatever that simple local infection like tonsillitis, as well as abscess of the aural cavities, infection of the postnasal space of the antra, and so forth, may be the port of entry. In some cases of this series the infection was implanted on an old endocardial or valvular scar. F. Billings (Arch. of Intern. Med., Nov., 1909).

Chronic infective endocarditis is pathologically unlike the ordinary ulcerative form, in that there are usually large, hard, firm, grayish-yellow vegetations projecting from the valves like warts, and in many cases an extension over the walls of the endocardium. This form has been called endocarditis lenta, as the symptoms may persist from six to thirteen months or longer. It is ushered in with a fever of the septic type (daily rising to 102.5° or 103° F.—39.2° or 39.4° C.), which may continue for six or seven months before the cardiac signs become pronounced. Chills may occur at intervals, but they may be entirely absent. Anemia occurs early and may lead us astray in our diagnosis. Embolic attacks are present in many cases and may give us the first hint as to the nature of the disease. Ephemeral cutaneous nodes are pathognomonic of this trouble—small, swollen areas about the hands or feet, or raised reddish nodes, like an ordinary wheal, painful but disappearing in a day or two. Organisms are found in the blood, a streptococcus known as *mitior* or *viridans,* because a poorly growing organism producing a green pigment on blood plates, associated sometimes with the influenza bacillus, the pneumococcus, and the staphylococcus. Vaccine treatment is of no avail in these cases. Osler (Interstate Med. Jour., Feb., 1912).

Of the 76 patients with chronic and recurring verrucous endocarditis at the Basel university medical clinic during the last four years, 16, that is, 21 per cent., recovered without any consecutive clinical functional disturbances. Even in cases in which a serious valvular defect was known to exist, the functional outcome was remarkably favorable. The verrucous affection involved the mitral or aortic valves, and in some cases not even at necropsy were evidences found of a cardiac defect, the lesions having healed smoothly. The cases were all of bacterial or bacterial-toxic origin. In some of the cases the heart cavities were somewhat enlarged and the heart a little heavier than normal, but these changes could be referred to factors outside the heart, contracted kidney, etc.

The patients were 15, 17, 20 and up to 79 years old. C. Amsler (Correspondenzbl. f. schweizer Aerzte, April 10, 1912).

ETIOLOGY AND PATHOLOGY.—Besides being a possible sequela of acute endocarditis, the chronic form may be produced through the influence of certain predisposing causes, namely: gout, alcohol, syphilis, and habitual muscular overexertion, particularly if in the individual there is a tendency to arteriosclerosis. Exceptionally, the wall of the heart itself is affected by the process, in which case it presents scar-like patches, which are often associated with myocarditis. There is also a form of chronic pneumococcic origin.

The organism of chronic pneumococcus endocarditis should be considered as a modified pneumococcus in that it produces an endocarditis by first causing an embolic hemorrhage which serves, in turn, as a culture medium for the organism. Growth begins then, before the leucocytes gain entrance to destroy the bacterial clump. A vegetation is the result. The writer holds that the form of endocarditis known clinically as subacute or chronic infections is due, in the vast majority of cases, to organisms of practically no virulence in the ordinary sense. Death is due to exhaustion, the result of prolonged parental protein intoxication. Rosenow (N. Y. State Jour. of Med., Aug., 1912).

Valves changed by chronic endocarditis are more or less opaque, thickened, and cicatricial or calcified. They may be contracted, deformed, curled up, and adherent by their edges to one another.

The chordæ tendineæ may likewise be involved in the morbid process and thereby be deformed, or fastened one to another, or greatly contracted so that the distorted valve is apposed to the muscular papillæ. The apices of the papillæ themselves may be more or less fibrotic. Fetal endocarditis is usually of this chronic form.

Case in a girl, 8 years old, in whom chronic endocarditis had first been noticed when she was 16 months of age. Her birth was normal and easy. She was breast-fed and was considered to be a normal child up to the age of 14 months, at which time the mother acknowledged that she had been fed indiscreetly. From 16 to 20 months of age she was very ill most of the time. It was then noticed that her heart beat very forcibly and she was taken to a physician. She was very short of breath, had moist râles in her chest, a certain amount of edema of the lungs, and she could scarcely walk across the floor. She was allowed to do as she wished. Finally she was put to bed and confined there for a number of weeks. When she was allowed to be up, her activities were very carefully supervised and she became very much improved. For instance, when going up stairs, she was requird to count ten on every step. Her fingers were not clubbed; she was now not suffering from any shortness of breath. A loud thrill was heard over the heart; there was but little hypertrophy, the apex being very near the normal point. W. B. Hoag (Amer. Jour. of Obstet., June, 1910).

TREATMENT.—The treatment of chronic endocarditis being that of the valvular lesions, will be described under the next general heading.

In the management of chronic endocarditis during the stage of compensation it is necessary, as emphasized by Stein, to individualize all cases, noting that every patient reacts differently to drugs, dosage, to different preparations of the same drug, and to different forms of mechanical stimulation. All compensation is, of course, relative. Alcohol should be dispensed with if possible, as also tobacco, tea, and coffee. All emunctories must be kept as nearly normal as possible. **Rest** in the recumbent position and **sleep** are all important. In cases with insomnia, **hydrotherapy** is of great value as a hypnotic and cardiovascular regulator. If drugs are used, **sodium and ammonium bromide** are less depressing than the potassium salt, while the **trional-veronal** group are of great service.

As nearly all **cardiac stimulants** act as vasoconstrictors, it is well to combine with them the **iodides** and **nitrites. Codeia** is, without doubt, the safest of the opium preparations when a stimulant and sedative is to be combined.

In chronic infectious endocarditis, absolute **rest, good air, sunshine,** simple but nourishing **food** and **tonics,** but avoidance of drugging are indicated. Here, even autogenous vaccine or sera are more harmful than beneficial.

> In chronic recurrent septic endocarditis, the treatment is mainly hygienic and dietetic, a liberal **diet** being indicated rather than the liquid or semisolid typhoid diet. **Hexamethylenamine, Credé's ointment, quinine,** and the like, while worthy of a trial, have in the main been useless. The **serums** and the **vaccines,** too, both the autogenous and the stock vaccines, have not given uniform results, most authors reporting unfavorably their use. The writer had 3 cases, 1 a gonorrheal case, terminating in recovery after an illness of six months, and 2 fatal cases, lasting three and six months, respectively. The former case was due to a streptococcus, but the antistreptococcus serum did not seem to be of any benefit. The last case due to the *Staphylococcus albus* showed no improvement after an autogenous vaccine. In this case, too, there was an embolus of the tibial arteries of the right leg which led to gangrene of the foot extending up to midway between the ankle and the knee. L. H. Hempelmann (Jour. Amer. Med. Assoc., July 6, 1912).

VALVULAR DISEASES OF THE HEART.

See the annexed colored plate for the leading signs of the various valvular lesions.

VALVULAR LESIONS.—Whether or not the abnormal state of the affected valve causes incompetence or obstruction, there results in either case an unnatural demand upon the muscular power of the heart. Thus, stenosis leads to an increased effort during systole of that cavity which is obliged to force blood through the narrow outlet, and a leaking valve permits blood to flow backward into the cavity which it has just left, and thus obliges it to do part of its work a second time. In either case, the affected cavity is made to contain a larger amount of blood than normal.

In case either auriculoventricular valve leaks, the corresponding ventricle receives, during diastole, a larger amount of blood than normal from the overdistended auricle.

The heart possesses reserve forces,

LEADING SIGNS OF ORGANIC HEART DISEASE. (SAJOUS.)

(See location of sounds in the opposite plate.)

MITRAL DISEASE. Most frequent of all.

Auscultation Center: fifth left interspace below apex, blue spot No. 1. Signs:—

Regurgitation.

1st sound *Ffoo;* radiates toward axilla and back.

2d sound *Dub;* obscured.

Heart is enlarged transversely. Apex blow displaced downward and more diffuse. Area of percussion dullness enlarged. Pulse small and irregular. Pulmonary congestion and dyspnea. Edema, ascites, cyanosis, etc., appear late.

Stenosis.

1st sound *Lub;* sharp and loud, or *Lub-Lub.*

2d sound *Frroo;* harshly radiates toward axilla and back.

Presystolic murmur. Apex blow slightly to left of normal, and sharply localized. Pulse small, but regular, except in advanced cases. Percussion dullness increased to right. Pulmonary congestion and dyspnea. Edema, ascites, cyanosis, etc., occur late.

Regurgitation and Stenosis.

1st sound *Ffoo;* radiating to axilla and back.

2d sound *Ffrroo, or ffroo-lup;* short and combined.

Pulse small, rapid, and irregular, alternating, sometimes dicrotic. Percussion dullness increased. Pulmonary congestion, dyspnea, and cough. Edema, ascites, cyanosis, etc., occur late.

AORTIC DISEASE. Next in frequency to mitral.

Auscultation Center: second right costal interspace, blue spot No. 2. Signs:—

Regurgitation.

1st sound *Lub.*

2d sound *Fffoo;* prolonged, sometimes double; may become harsh *Frroo;* radiates upward into carotids and sometimes downward.

Pulsating arteries of neck characteristic. Systolic shock heard in brachial and other arteries. Corrigon or "water hammer" pulse; rapid, abrupt, and poorly sustained. Apex impulse forcible, heavy, and lowered to the left. Percussion dullness increased toward left.

Pallor characteristic; vertigo and sometimes syncope. Edema, ascites, hepatic congestion, etc., occur late.

Stenosis.

1st sound *Fffoot;* prolonged whistling and harsh; radiates upward into carotids; sometimes downward.

2d sound *Dub;* weaker than normal.

No external pulsations. Displacement of heart; apex removed downward and to left. Pulse not heaving or bounding and less collapsible; sometimes hard. Palpitations.

Regurgitation and Stenosis.

signs of both conditions may prevail.

1st sound murmur most marked and radiates into carotids.

Dyspnea, due to passive pulmonary congestion; cyanosis and dropsy occur early.

TRICUSPID DISEASE. Occasionally complicates mitral disease or dilatation.

Auscultation Center: lower end sternum, blue spot No. 3. Signs:—

Regurgitation.

1st sound *Fee-oo;* radiates toward left nipple.

2d sound *Dub.*

Venous pulse in neck; pulsating, congested liver. Percussion dullness increased to right. No effect on pulse. Edema, ascites, etc., occur early.

Stenosis. Very rarely observed.

1st sound *Lub.*

2d sound *Ffrroo;* harsh rolling; radiates toward left nipple.

Venous engorgement visible in neck without pulsation. Congested liver. Percussion dullness increased to right. Pulse small. Cyanosis, dyspnea, edema, ascites, etc., occur early.

PULMONARY VALVE DISEASE. The rarest of heart lesions.

Auscultation Center: second left costal interspace, blue spot No. 4. Signs:—

Regurgitation.

1st sound *Lub.*

2d sound *Ffoo;* radiates upward to clavicle.

Inspiration sounds in lungs interrupted. Apex beat moved somewhat to left. Percussion dullness increased to right.

Stenosis.

1st sound *Ffrroo;* rough; radiates upward to clavicle, but widespread.

2d sound weak or absent or replaced by diastolic murmur.

Cyanosis an early sign; tendency to hemorrhages. Varicose dilatation of peripheral veins. Percussion dullness increased to right. Edema, ascites, etc., occur very early.

Occasionally met with in infants and tuberculous subjects.

Regurgitation and Stenosis.

Extremely rare. Signs of both lesions combined.

ENDOCARDITIS.

Signs according to the valvular structures involved; those of insufficiency or stenosis, as above, appearing in turn or together. At first soft, gradually become rough, sibilant, and grating. Signs recede as the case improves, unless chronic organic lesions engendered. Apex beat moved slightly to left. Percussion dullness slightly increased.

PERICARDITIS.

Before Effusion. Friction murmur. Close to ear when patient sits up and therefore clearer; recedes when patient lies down. Coincides with heart sounds and does not radiate into vessels of neck. Presystolic murmur sometimes heard at apex. Percussion dullness normal. **Yellow outline, No. 5.**

With Effusion. Serum gradually fills pericardium; hence heart sounds, or murmurs, distant or lost and area of dullness increased, according to quantity of fluid present. Area finally becomes pyriform. Apex stroke against chest wall lost. Absorption of fluid indicated by return of murmurs beginning above and increasing as level of fluid descends, and clearing of heart sounds. **Yellow outline, No. 6.**

MYOCARDITIS.

Acute Form. Heart sounds short, sharp, tumultuous, then become feeble. Valvular murmurs brought on by disease of heart muscle and sometimes by dilatation. Endocardial changes indicated by an increased pulmonary second sound.

Chronic Form. Impulse feeble and heaving. Apex stroke displaced downward and to left. Heart beats often greatly decreased in number and often intermittent. Attacks of angina pectoris and palpitations. Lesions of mitral valve frequently appear with gallop rhythm.

HYPERTROPHY.

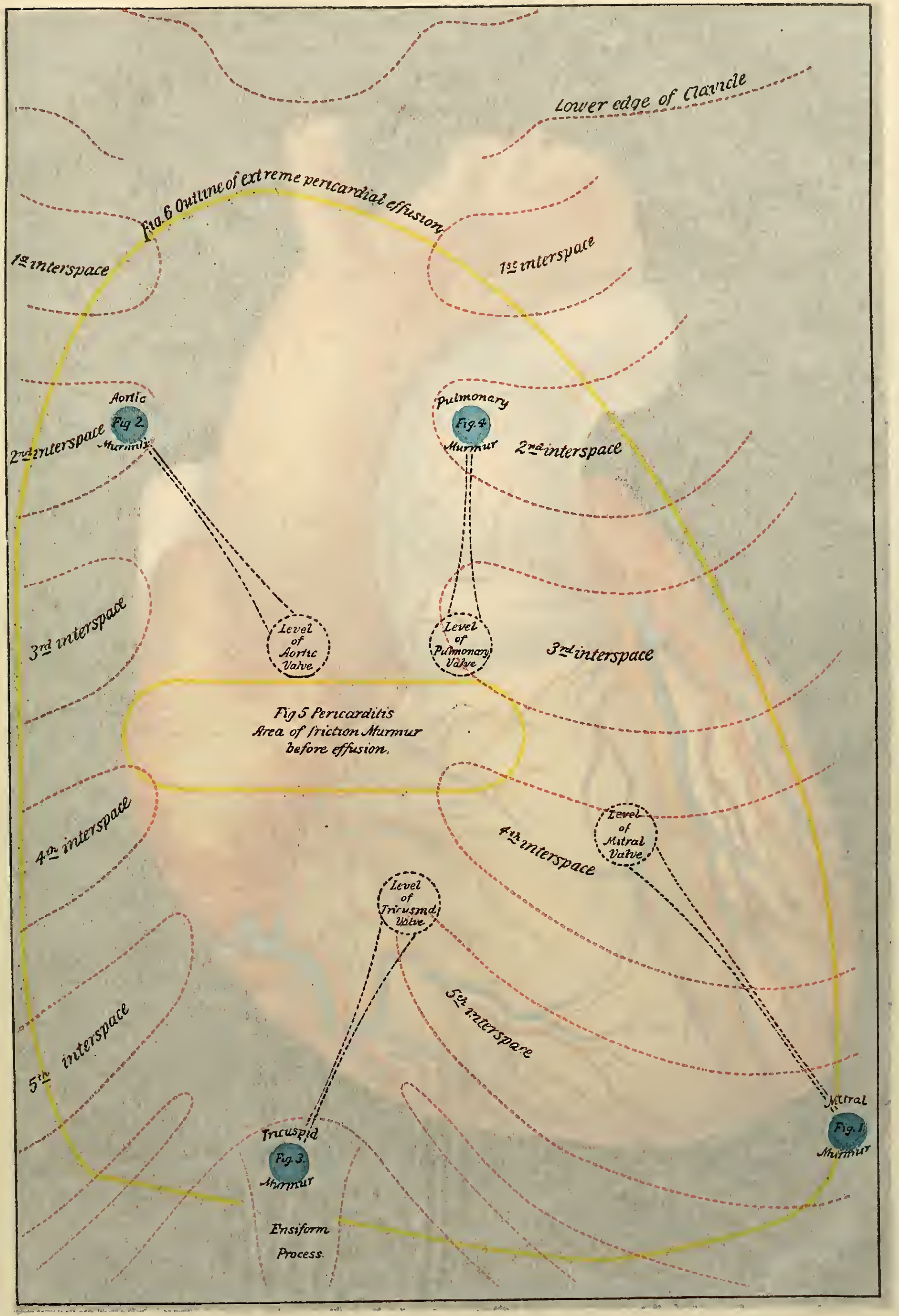
All heart sounds increased, especially aortic second sound. Irregular gallop rhythm in marked cases. Action heaving and vigorous: *booming.* Impulse at apex hard and diffuse. Murmurs indicate coexisting valvular lesions.

DILATATION.

Signs of tricuspid insufficiency (see above). First sound short, sharp, and ringing. Venous pulsations in the neck and venous turgescence. Epigastric pulsation. Percussion dullness extended to the right. Pulse small, irregular, and rapid.

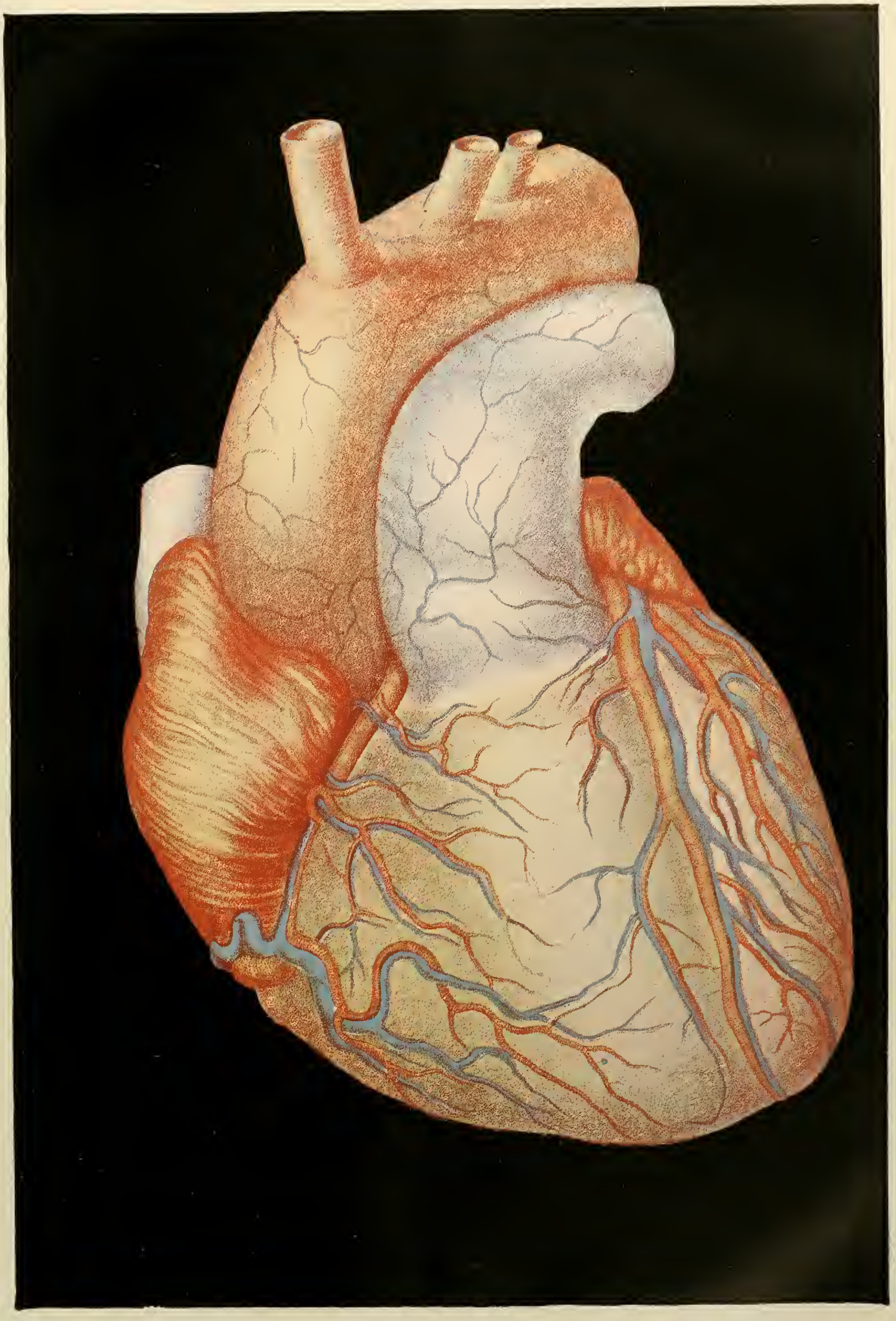
FATTY HEART.

No characteristic sign except weakened heart action. When other signs appear they are those of dilatation (see above).



Section of Chest Over the Heart, Showing the Location of Cardiac and Pericardial Sounds. *(Sajous.)*

The blue spots indicate where the normal valvular sounds are detected stethoscopically. The yellow outlines indicate the relative area of extreme pericardial effusion.



and, while the immediate effect of a valvular lesion is dilatation of the chamber affected, the secondary result is hypertrophy of the muscular walls, and a more or less complete fulfillment of the new demands. Unfortunately, however, there is for several reasons a tendency to retrogression. In the first place, the valvular endocarditis may grow worse by slow change or because of a recurrent acute inflammation. Secondly, the myocardium is apt to deteriorate so that the muscular power of the heart diminishes. Thirdly, in some forms of valvular disease, particularly aortic, the coronary arteries from which the heart derives its nourishment are apt to be involved. The period during which the heart, having hypertrophied, remains equal to the demands made upon it is called the period of "compensation." Sudden exertion, great mental excitement, or the stress of intercurrent disease may cause a temporary "disturbance" of this compensation. Finally, extreme degrees of valvular deformity and myocardial degeneration bring about "ruptured compensation."

MITRAL REGURGITATION.

DEFINITION. — Insufficiency of the mitral valves, permitting blood to leak into the left auricle during systole.

SYMPTOMS.—The subjective symptoms of mitral regurgitation depend upon the degree of compensation present in the individual case. Thus, if the condition is a favorable one, the patient may be unconscious of any unnatural state whatever, having no dyspnea except on considerable physical exertion. On the other hand, if the circulation is beginning to be embarrassed, we may observe palpitation, shortness of breath on exertion or excitement, cyanosis and, perhaps, edema of the dependent parts. On physical examination the heart is found to be enlarged mainly in its transverse diameter, the apex being pushed toward the left, and the limit of dullness extending farther toward the right than in health. The cardiac impulse may be more diffuse than in health, and visible in the epigastrium as well as in the normal position. In young subjects the precordia may be somewhat bulged. On palpation, a systolic thrill may sometimes be distinguished; this is not, by any means, the rule, however. On auscultation, we hear at the apex of the heart a murmur systolic in time and transmitted outward toward the axilla. This murmur is also audible inside the lower angle of the scapula. At the base the pulmonic second sound is accentuated and often reduplicated. The pulse in well-compensated cases may be nearly normal. In later stages it is rather small, frequent, of low tension, and irregular in force and rhythm.

The significant symptoms of failing compensation, dyspnea, cough, and hemoptysis sometimes appear before the physical signs. The gradual disappearance of a murmur and gradual weakening and final disappearance of the apex-beat have an evil significance. In cases of mitral disease a well-marked accentuation of the second sound in the pulmonary area is a favorable sign, indicating vigorous action of the right ventricle. In connection with symptoms of failing compensation it is of importance to decide whether the breakdown is due to simple overstrain and exhaustion of the heart and is, therefore, capable of being recovered from, or whether it depends on definite and irremediable organic changes in the myocardium. Carr (Practitioner, Sept., 1907).

DIAGNOSIS.—The important factors in diagnosis are, first, the systolic murmur, which is usually heard loudest at the apex and transmitted outward, and which, in some instances, may be heard over a much more extensive area; in fact, almost all over the chest. Again, the murmur may be audible merely along the left edge of the sternum. The sound is of a blowing character, sometimes musical, especially toward its termination, and it replaces the first sound of the heart to a greater or less extent.

The second factor in diagnosis is the transverse enlargement of the heart. The apex may be lowered into the sixth space, but the main change is in the width of the cardiac dullness, which may extend from the left anterior axillary line to the right nipple.

Third, the pulmonic second sound, heard in the second left space or over the third left costal cartilage, is accented and perhaps reduplicated. Relative insufficiency of the mitral valve, with a normal condition of the valves, but with such dilatation of the left ventricle as to prevent the closure of the mitral orifice, may give rise to a precisely similar trio of signs.

It has been claimed that the only means of making the diagnosis of valvular incompetency as distinguished from relative insufficiency would be to find, in addition to the other signs, a presystolic murmur due to accompanying stenosis of the diseased valve. In many cases the history of the disease and the general appearance of the patient would be equally decisive. Functional or hemic murmurs may be heard during systole at the apex and transmitted outward, but they are not associated with enlargement of the heart or accentuation of the pulmonic second sound.

ETIOLOGY.—Deformities of the mitral valve leading to incompetency are caused by acute endocarditis, and still more frequently by chronic fibroid change. Relative incompetency of the mitral valves may be due to failing compensation in case of an aortic lesion; or to the terminal stage of idiopathic hypertrophy of the heart (meaning that condition of the myocardium which is seen after habitual excess in muscular exertion and in the use of alcohol); also to changes in the heart secondary to chronic nephritis, arteriosclerosis, and chronic adhesive pericarditis.

PATHOLOGY.—The diseased valves present characteristic changes. They are more or less opaque, thickened, and cicatricial or calcified, and as a result contracted, curled, or otherwise deformed. The edges of the valve segments and of the chordæ tendineæ to which they are attached are frequently more or less adherent one to another. In advanced stages the valvular orifice may be transformed into a rigid, calcified ring. The mechanical effects of mitral regurgitation are as follows:—

During systole blood escapes backward through the valve into the left auricle, which cavity, therefore, receives blood both from normal sources and from this new abnormal one. Consequently the left auricle becomes dilated, and, as a consequence of the new demands made upon it, hypertrophied, so that its walls may be three or four times the normal thickness. Moreover, the left ventricle receives with each diastole not only its normal quantity of blood, but an abnormally great amount from the dilated and hypertrophied left auricle; so that it also becomes dilated and hypertrophied. As the valve lesions become aggravated, or the strength of the left auricle diminishes, the flow of blood from the pulmonary veins into the left auricle becomes impeded and the whole pulmonary circuit congested, thus putting a strain upon the right ventricle. It is the hypertrophied right ventricle which is the main factor in preserving a normal flow of blood in case of mitral regurgitation. At last the right ventricle fails,—dilates; the tricuspid valve becomes relatively incompetent; the right auricle is embarrassed, and finally the systemic circulation becomes congested.

> The physiology of cardiac action and blood-pressure based on the statistics at Guy's Hospital, London, of cases of hemoptysis occurring in valvular disease, raises doubts as to the existence of any great increase in pulmonary blood-pressure in cases of simple mitral incompetence. While there is no doubt that the pulmonary pressure is raised both in mitral stenosis and incompetence, it becomes a question why hemoptysis is so much more frequent in stenosis. There is this distinction, therefore, between the increased pulmonary tension of mitral incompetence and that of stenosis: The pressure is raised in both lesions during ventricular systole, but in the former it may be relieved immediately on the completion of the systole during the period of relaxation that takes place before the semilunar valves close, while in stenosis the increased pressure persists well into the diastole and, hence, in this latter condition the signs of high blood-pressure in the pulmonary circulation are more marked. Kerr (Calif. State Jour. of Med., Aug., 1907).

Patients with mitral regurgitation before the advent of the subjective symptoms may be seen to be slightly cyanotic, and young subjects are apt to have clubbing of the ends of the fingers. As compensation fails, the lungs become congested and edematous and undergo brown atrophy; the liver, spleen, and kidneys present the lesions of passive congestion, the lower extremities begin to be edematous, and finally general dropsy and orthopnea appear.

PROGNOSIS.—Mitral regurgitation may exist for years without subjective discomfort, particularly if the patient escapes any great nervous or physical stress in life. Moreover, when compensation is impaired, judicious treatment will repeatedly restore the patient to a state of comfort. Finally, of course, the embarrassment cannot be alleviated and death ensues; but death is apt to be gradual rather than sudden.

TREATMENT.—With regard to treatment, much which is applicable to this subject will be given in the next volume, in the section upon DILATATION OF THE HEART, and other considerations will be discussed at the end of the section on VALVULAR DISEASES.

MITRAL STENOSIS.

DEFINITION.—Mitral stenosis is a change in the mitral valves which impedes normal flow of blood from the left auricle into the left ventricle.

SYMPTOMS.—Many individuals present this lesion without being conscious of ill health. They may experience a certain amount of shortness of breath upon exertion, but do not suspect the existence of cardiac mischief. Some patients are of a tolerably fresh complexion and do not suggest the idea of cardiac difficulty, but rather of chlorosis; such patients, so far as the writer's experience goes, are rather slight and undersized. The great majority of sufferers are women. Some cases are supposed to be congenital, but this must be exceptional. As compensation fails, we have the usual train of cardiac symptoms, with the difference that pulmonary engorgement, bronchitis, passive congestion of the lungs, orthopnea, and hemoptysis are more common with this than with other valvular lesions because of the direct way in which it impedes the pulmonary circuit.

> False mitral stenosis may occur in the anemic owing to excessive functioning of the heart, the signs and symptoms of which simulate those of true organic mitral stenosis. It is differentiated from the latter by the variability in the symptoms, the coexistence of nervous disturbances and signs of anemia, the duration of the systolic sound and, above all, by the absence of any delay in the radial pulse and duplication of the second sound. Radioscopy will confirm the absence of the enlargement of the left auricle of organic mitral stenosis. The prognosis in these cases of pseudostenosis is favorable unless the patient has a tuberculous taint, in which case there is possibility of its transformation into the true organic form. J. Teissier (Riforma Medica, April 10, 1911).

DIAGNOSIS.—As already stated, the disease may be unsuspected until a physical examination is made. Upon inspection of the chest, we may observe the apex beat, displaced slightly to the left. The lower part of the sternum and the apex region may be somewhat prominent in children, and an impulse may be seen with the systole in the fourth and fifth left space, due to the hypertrophied right ventricle.

> In rare cases of mitral incompetency the systolic murmur may be heard exclusively in the left chest at the back, in the region of the angle of the scapula, at least for a certain length of time. Ortner (Med. Klinik, Nov. 1, 1908).

Upon palpation near the apex, usually somewhat inside of it, may be felt a remarkable purring thrill, which will be found to be presystolic in time and to terminate with a distinct shock corresponding to the beginning of cardiac systole. This shock may be felt over three or four intercostal spaces to the left of the sternum. Its origin is a matter of considerable speculation, but not as yet of demonstration.

On percussion the cardiac area will be found to be increased transversely to the right of the sternum. On the left it often reaches somewhat higher than normal, but laterally not much beyond the normal limits.

On auscultation at or inside the apex is heard a presystolic murmur of a characteristic quality. It is more or less rubbing, rumbling, or churning, and terminates with a sharp valvular sound corresponding to the shock felt by the hand. Immediately following this sound, if the case is one of pure mitral obstruction, is a brief pause, and then a fainter valvular sound is heard corresponding to the second sound of the heart.

> A study based upon the results of simultaneous records taken by a microphone and a string galvanometer, showed that in mitral stenosis the diastolic murmurs are due to the rapid outflow of blood through the stenosed mitral orifice. Murmurs occupy those periods of diastole during which the velocity of outflow reaches a certain grade. When the auricle contracts at the normal time and the heart beats slowly, the velocity tends to be greatest in presystole; otherwise it is usually greatest in early diastole, and these are the periods at which the murmurs are most commonly audible. Lewis (Brit. Med. Jour., Dec. 21, 1912).

If the case is one of stenosis and regurgitation combined, the first sharp valvular sound is followed by a systolic murmur.

The character of the typical presystolic murmur of mitral stenosis is so distinctive that it would seem to the writer possible to establish a diagnosis of mitral stenosis upon this sound alone without other evidence.

> Case of mitral stenosis in which the presystolic murmur was constant and persisted during those cycles in which there was ventricular silence, the irregularity being due probably, to *digitalis poisoning.* In this case the murmurs which accompanied ventricular contraction, together with the first and second sounds, were wanting, the presystolic murmur alone marking the occurrence of the cycle.
>
> The writer witnessed a second case of mitral stenosis, with a presystolic murmur, in which there are no cardiac irregularities. After admission to the hospital the patient was treated from time to time with tincture of strophanthus and the tincture and infusion of digitalis. During the time of the digitalis poisoning, an irregularity was noted which on analysis proved to be similar to that of the first case. A. E. Cohn (Jour. Amer. Med. Assoc., May 21, 1910).

At the base of the heart in the second left space is heard a sharply accented and usually reduplicated sound, corresponding to the closure of the pulmonary valves under tension.

In cases of failing compensation, the thrill may be difficult to feel. It may sometimes then be perceived by apposing the palm of the hand lightly to the chest wall, when a very faint and extremely circumscribed thrill may be detected. With a dilated heart the auscultatory sounds also are indistinct. It may be impossible to recognize the existence of mitral stenosis in a patient seen then for the first time. If, however, compensation be restored wholly or in part, the murmur may reappear. The time of the murmur may be postdiastolic or middiastolic rather than strictly presystolic. The pulse is small and irregular. When compensation fails, it becomes weak, frequent, more irregular, and intermittent.

> A study of pure mitral stenosis in 200 cases showed that incipient, rudimentary mitral stenosis escapes detection by ordinary inspection and palpation, but that it is possible to differentiate it even in its earliest stages by various signs and symptoms. These include the displacement of the wave of the apex beat to the left (which was found in 91 per cent.) or to the left and upward (5 per cent.); slight reduction in the passive mobility of the heart (55 per cent.); displacement upward of the apex when the patient changes from the reclining to the seated position (73 per cent.); the beat more extensive in the transverse sense (88 per cent.); the beat a little more pronounced than normal (7 per cent.); the beat arrhythmical (51 per cent.) or a double impulse at the apex (5 per cent.); absence of the physiologic negative pulsation (25 per cent.); diffuse shock in the lower half of the sternum; well-marked pulsation at the left and right margins of the sternum; cardiac impulse in the epigastrium (97 per cent.); in the lung region (33 per cent.); the auricular cardiac impulse of Grocco (15 per cent.); diastolic valvular shock over the pulmonary; presystolic or diastolic-presystolic thrill at the apex; Brun's dull pain at a point in the epigastrium, below and to the left of the xiphoid appendix, the continuous vague pain here being exaggerated by pressure and sometimes becoming sharp and radiating to the region around the umbilicus or the entire abdomen or in a girdle radiating to the lower part of the back; Vaquez's auricular tender point is the result of enlargement of the auricle. The pain here develops spontaneously at different points or can be elicited by pressure. The patient complains of vague discomfort in the back, but locates the seat of the pain on demand in the region between the spine and the spinal margin of the left scapula. In conclusion the writer expatiates on the great diagnostic importance of the zones of Head in differentiation of pure mitral stenosis, and gives the

details of 5 cases in which these zones were particularly in evidence. Landolfi (Jour. Amer. Med. Assoc., from Riforma Medica., April 27, 1912).

Tricuspid stenosis may give rise to a presystolic murmur, situated to the right of the sternum; but this disease is extremely rare unless congenital, and when it does occur is apt to be secondary to chronic lesions of the left side of the heart. Persons born with tricuspid stenosis are apt to be simultaneously affected with other abnormalities which entail speedy death.

The late Austin Flint called attention to the presystolic murmur frequently heard in cases of aortic regurgitation at the apex of the heart, and ascribed it to the influence of the blood-current falling into the left ventricle through the incompetent aortic valves. This murmur is associated with the ordinary signs of aortic regurgitation and is not accompanied by the peculiar thrill felt in mitral stenosis; nor is it followed by the systolic shock above described.

There are two valvular affections of the heart which may give the impression of an aortic aneurism. The first, aortic insufficiency, as Corrigan pointed out, suggests it by the marked pulsation of the arch of the aorta. To the paroxysms of cyanosis and dyspnea may be added a visible pulsation in the second left interspace close to the sternum and a paralysis of the left vocal cord. Ortner (of Vienna) was the first to describe the compression of the left recurrent laryngeal nerve between the aorta and a considerably dilated left auricle, in a patient in whom he had diagnosticated aneurism *intra vitam.* The majority of the cases have such a cause, but some few are due to compression by enlarged pulmonary veins or the left pulmonary artery. The writer witnessed 3 cases, 2 of which were with autopsy. All 3 had signs of a double mitral lesion and paralysis of the left vocal cord. Autopsy in 2 of the cases showed the recurrent laryngeal nerve sclerotic and opaque in the portion compressed between the wall of the left auricle and the aorta. Osler (Arch. d. mal. cœur, d. vaisseaux et d. sang, vol. ii, p. 73, 1909).

There are now on record 11 autopsied and 26 clinically reported cases in which recurrent laryngeal paralysis was associated with and apparently the result of mitral stenosis. Among the autopsied cases the vocal paralysis was attributed to direct compression on the part of the auricle or its appendix in 7; to cardiac displacement, traction, etc., in 1; to the effects of a persistently patulous ductus arteriosus in 2; and to indirect compression acting on the pulmonary artery in 2. It is the authors' conviction, based on careful study of the anatomical relations in hardened preparations, that the indirect mechanism may be a variable one, but that when compression is accountable for the recurrent paralysis, it must always be caused by the nerve being squeezed between the left pulmonary artery and the aorta or the aortic ligament. Anything which will dilate or force upward the left auricle, the left upper pulmonary vein, or the left pulmonary artery would tend to cause the condition. Fetterolf and Norris (Amer. Jour. Med. Sci., May, 1911).

ETIOLOGY.—Rarely the lesion may be congenital. In most instances it is the result of valvular endocarditis due to rheumatism or chorea or some other of the children's diseases. Anemia and chlorosis have also been thought to have some influence in promoting its occurrence.

Pure mitral stenosis is an independent valvular defect which generally develops between the ages of 10 and 30 as a result of endocarditis. It may be congenital or functional, but only in the rarest cases. The female figure, especially when there is a tendency to weakness and hypoplasia, seems to favor the development of this form of valvular defect. It consequently occurs mainly in girls and is distinguished by its relative harmlessness, although the patients rarely live to an advanced age. Hampeln (Deut. Arch. f. klin. Med., Bd. cv, Nu. 5-6, 1912).

PATHOLOGY.—Mitral stenosis is almost invariably associated with a greater or less degree of mitral regurgitation. By itself, mitral stenosis does not cause much enlargement of the heart. The left ventricle may be of normal size or smaller. The left auricle and right ventricle are, however, much dilated and hypertrophied. The valves may be changed to a variable extent. In the most extreme cases the auriculo-ventricular orifice is scarcely big enough to admit the head of a pin. The left auricle often contains thrombi. Sometimes the great enlargement of the left auricle causes pressure paralysis of the left recurrent laryngeal nerve—the same lesion which is caused, more often, by thoracic aneurism.

In a series of 50 cases which came to autopsy, the cardiac lesion was confined in 25 cases to the mitral valve; in 7 others the mitral lesion was the chief finding, but was combined in 2 with chronic fibrous pericarditis and in 5 with inflammation of the aortic valves. Aortic stenosis complicated 9 other cases, aortic insufficiency 3, and tricuspid stenosis 6. In 4 of the latter aortic regurgitation was also present. G. G. Sears (St. Paul Med. Jour., March, 1907).

PROGNOSIS.—As already stated, mitral stenosis is not incompatible with a tolerable degree of health, and may not for years call attention to itself. Even after compensation has been impaired, great improvement may be repeatedly obtained by suitable treatment. On the whole, the disease may be said to be somewhat less favorable than is mitral insufficiency. Yet, of this, as of every cardiac lesion, it should be said that the prognosis depends upon the peculiarities of the individual case, which should be considered upon its own merits.

TREATMENT.—The treatment is considered at the end of the section on VALVULAR DISEASES, page 500, to which the reader is referred.

AORTIC REGURGITATION.

DEFINITION.—A lesion of the aortic valves allowing a reflux of blood into the left ventricle during diastole.

A patient with free aortic regurgitation may for years lead an active life unconscious of his condition. In no other valvular disease is compensation, while it lasts, so perfect. If, however, the lesion develops abruptly, it will produce marked symptoms. For instance, when it is consequent upon the sudden rupture of a segment of the valve during violent physical exertion, or when the valve is perforated by the ulcers of malignant endocarditis, the heart may be almost or completely overwhelmed by the sudden strain put upon it, the left ventricle dilating and thus causing relative insufficiency of the mitral valve, engorgement of the lungs, and an embarrassment of the whole circulatory apparatus, from which the patient can scarcely recover.

In some instances the first shock is successfully endured, and a slow development of the reserve power of the heart establishes compensation. This happier result was observed by the writer in the case of a Western miner in whom the aortic lesion developed overnight.

The commonly accepted view that mitral disease is by far the most frequent of the valvular lesions of the heart should be modified. From his experience in private practice, as well as with extensive hospital material, the writer believes that aortic lesions are fully as frequent or more so than lesions of the mitral orifice. From the records of the Cincinnati Hospital for four years, from 1900 to 1903 inclusive, it was found that, in 160 autopsies with well-defined heart lesions, aortic diesase and mitral disease were about equally distributed, with a slight margin in favor of the greater frequency of the former. Admitting that the infection, as seen in acute articular rheumatism, more frequently affects the mitral area, the fact remains that the severest type of the so-called ulcerative endocarditis does greatest damage to the aortics. Especially in syphilis, is the tendency to aortic lesions pronounced. J. E. Greiwe (Jour. Amer. Med. Assoc., March 9, 1912).

SYMPTOMS.—Where compensation has been perfect and is beginning to fail, the first symptoms may be cerebral, such as dizziness, flashes of light, and slight headache; there may also be faintness and palpitation on slight exertion. A patient seen by the writer had for his first symptom a sharp neuralgic pain in the lower jaw which developed while he was carrying a canoe on his back through the woods of Maine. Pain may be very prominent. It is usually precordial, but may extend into the neck and down the arms, particularly the left arm. Angina pectoris may occur, and in no form of valvular disease is sudden death more common than in this.

Compared with mitral lesions, there is less apt to be cyanosis, bronchitis, or anasarca; more apt to be head symptoms and pallor. Embolism may occur, and slight febrile attacks are not uncommon, either due to recurrent endocarditis or in some instances to articular rheumatism. In this and in other valvular lesions there may be delirium toward the close of life.

It is also stated that there seems to be some connection between mental diseases and cardiac lesions even when well compensated. With regard to this the writer has had no practical experience. It is usually said that the cardiac psychoses are apt to be of a melancholy character. Savage says: "With aortic or with both aortic and mitral disease, the symptoms may be either melancholic or maniacal; but I am inclined to think that, with simple aortic disease and with hypertrophy of the left ventricle, it is at least not uncommon to meet with acute mania and exaltation of ideas."

Aortic regurgitation sometimes occasions cerebral hemorrhage, and pericarditis sometimes complicates disease of the aortic valves, whether stenosis or regurgitation.

Upon physical examination it is usually easy to recognize aortic insufficiency if it exists. Inspection shows an extensive and powerful cardiac impulse. The apex is seen to be in the sixth or seventh intercostal space in the nipple line or outside, and the chest wall may be prominent over the hypertrophied left ventricle. Upon palpation, the powerful action of the heart is evident, and exceptionally there may be a diastolic thrill. In this disease the heart may attain its largest dimensions.

Temporary aortic leakage is not so uncommon as is usually held by clinicians. More attention should be paid to the atypical forms which a murmur may assume. The capillary pulse is the most constant sign, and its frequency in other lesions is probably greatly overestimated by reason of the fact that an existing aortic regurgitation may be readily overlooked. A capillary pulse in neurasthenic patients is frequently attributed to the neurasthenia rather than to its true cause. A modification or absence of the second carotid tone is a most valuable and constant sign in cases unassociated with marked arteriosclerosis. No examination having reference to the integrity of the heart is complete unless the carotid tones and capillary pulse are carefully investigated.

C. L. Greene (Archives of Diagnosis, April, 1908).

Upon auscultation, there is heard a diastolic murmur, which may be loudest in the second intercostal space on the right, or in the third or fourth space at the left edge of the sternum. Exceptionally it may be heard best at the left side near the xiphoid cartilage. This murmur is of low pitch, and of a blowing character, and it may replace the second sound of the heart. If not, it begins immediately upon the occurrence of that sound. No cardiac murmur is audible over so extensive an area as may be that of aortic regurgitation. It may be heard all over the chest, and in the brachial and femoral arteries. In some cases it is difficult of detection, and, when this or any valvular lesion is suspected, it may be laid down as a general rule that no examination is complete unless auscultation has been carefully practised when the patient was in a horizontal and also in a vertical position.

Sometimes the murmur can be heard best with the naked ear applied to the uncovered chest wall. Exceptionally the murmur may be heard only at the apex of the heart, and in this connection the murmur described by Flint, presystolic in time and heard at the apex, should be borne in mind. This has been already described in discussing the diagnosis of mitral stenosis. Flint's murmur is of a blubbering character, and heard only over a limited area at the apex. The sound heard at the base of the heart is usually rather long; when it is short and gushing there is (it is claimed) reason to infer an extensive lesion. It is stated that it is also unfavorable to find the murmur audible only in the midsternal region. Sometimes the murmur has a distinctly musical quality. This is explained as due to the perforation of a valve segment in such a way that a thin strip of valve is left intact and made to vibrate by the regurgitating blood. Frequently there is an accompanying systolic apex murmur, due to relative incompetency of the mitral valve, although, of course, it may be a sign of coexistent mitral disease. Usually there is at the base a systolic murmur, and this occurs independently of aortic stenosis. One explanation of its development is that the first outflow of blood from the contracting ventricle meets the still regurgitating current falling through the incompetent valve, and thus gives rise to the murmur.

The diastolic murmur may sometimes be heard, as already stated, in the peripheral arteries. Sometimes the second sound of the heart may be heard in the carotid when not audible at the base of the heart. If so, its interpretation is favorable as implying a lesser lesion of the aortic valves. Sometimes a systolic and diastolic murmur may be heard in the femoral and other arteries (Duroziez). This is obtained by a slight pressure with the stethoscope, and is due to the outward current of blood causing a systolic and the returning blood a diastolic sound at the place of artificial stenosis. This is a very important diagnostic factor when found, but it is not always present in aortic regurgitation.

The point of maximum intensity of the aortic diastolic murmur is not constant, but varies under different conditions, most authorities placing it in the third and fourth interspace to the left of the sternum and near its margin. The writers, having noticed the frequency of a diastolic murmur at the apex and in the axilla, made a careful study in a number of cases of aortic insufficiency as regards these points of transmission. In all but 2 of 17 cases examined the diastolic murmur was heard outside the apex in the axilla. At times the murmur in the axilla may be of secondary or even, as in 2 cases of maximum intensity, that is, in passing from the point of maximum intensity close to the sternal border, the murmur diminishes in intensity as the apex is reached and then becomes louder in the axilla. This axillary murmur is of exactly the same kind and quality as that heard at the base, and should be identified as the "aortic axillary diastolic" murmur. R. Cole and A. B. Cecil (Johns Hopkins Hosp. Bull., vol. xix, p. 353, 1908).

Aortic insufficiency without murmur can be diagnosticated by palpation, when the vaulting shock will be noted, that is, a dome-shaped elevation of the region of the apex at each aortic impulse without valvular vibration. This shock is permanent, somewhat circumscribed but well defined; in the dorsal decubitus of the patient the shock is to be found in the fifth intercostal space; in the left-sided position of the patient it is more pronounced and is to be located in the sixth intercostal space. LeBard (Semaine méd., June 2, 1909).

If one finds by auscultation, together with a systolic murmur *ad aortam,* a well-preserved, often sharply accentuated, second aortic sound, an insufficiency of the aortic valves is excluded; and if one hears, most clearly when the patient is lying down, but usually when he is standing also, a soft diastolic murmur in the third left intercostal space, it indicates with the greatest probability a dilatation of the arch or of the descending portion of the aorta. Stein (Münch. med. Woch., Sept. 7, 1909).

Leonard Hill noted that in aortic regurgitation there is remarkable difference in systolic pressure found in the arm and leg, the pressure in the lower limb being often extraordinarily high, not rarely amounting to 100 millimeters of mercury above that of the upper extremity. The writer found, in making comparative studies of the blood-pressure in the arm and leg of cases of aortic regurgitation, not only confirmed Hill's conclusions, but gave even greater variations than he records, and that this extraordinary difference between the systolic pressure in the arm and leg is a pathognomonic sign of aortic incompetence, as it is not present in other valvular lesions. H. A. Hare (Therap. Gaz., July, 1910).

The femoral artery, and also the smaller arteries, such as the dorsalis pedis and the radial, usually afford a peculiar, sharp, valvular "pistol-shot" sound with each cardiac systole. This sound may exceptionally be doubled.

The pulse is characteristic. It has been called the "water-hammer" pulse, or the "Corrigan" pulse, after Corrigan, who admirably described it, or the "shuttle" pulse. It is very quick and abrupt, and is extremely ill-sustained. These characteristics are more evident if the arm is raised vertically, and they can be well appreciated by grasping the wrist with the hand (Osler) instead of by the ordinary mode of palpation with the finger. In this disease there is also a capillary pulse: a phenomenon which may also be observed in neurasthenia and profound anemia, but much less often. It can be seen in the nails, in the vessels of the retina through the ophthalmoscope, upon a surface artificially reddened by firm rubbing, as on the forehead, and it may also be well observed through a glass slide placed upon the everted lower lip. It consists of an alternate flushing and paling of the part, corresponding with the sudden filling and emptying of the vessels.

In rare instances there is even a centripetal venous pulse, seen best on the back of the hand.

The writer examined 24 patients with grave aortic insufficiency, and found circulatory hippus in one of them. The patient suffered from arteriosclerosis with aortic insufficiency and hypertrophy of the left ventricle. A rapid alternate contraction and dilatation of the pupil was observed. He also noted this sign in 3 other patients after giving 15 drops of tincture of digitalis a day for four days. Landolfi (Semaine méd., July 28, 1909).

DIAGNOSIS.—As already stated, persons may have aortic regurgitation without symptoms; hence the disease may sometimes be discovered only upon physical examination. When the signs above enumerated have been detected, there is scarcely any doubt about the diagnosis.

A diastolic murmur at the base of the heart may be occasioned by an enlargement of the aorta, due to aneurism, but this lesion would have a different history and would present other signs peculiar to itself. Moreover, aneurism usually gives a systolic, rather than a diastolic, murmur. Examination with the X-ray would be conclusive.

Insufficiency of the pulmonary valves is a very rare lesion, and, if present, the murmur caused by it should be transmitted downward and to the right, and there would be no hypertrophy of the left ventricle or "water-hammer" pulse.

Patency of the ductus arteriosus is a rare condition, and the murmur associated with it has been described as "late systolic" or, again, as "continuous with the second sound, transmitted only very feebly to the left, and of a wavy character, sufficient of itself to distinguish it from an aortic regurgitant murmur."

The causes of degenerative lesions producing aortic regurgitation in old age are (1) senile degenerative change, (2) high arterial tension or constant strain on the valves and arch of the aorta, (3) severe intermittent strain on the valves from frequent and violent fluctuations in the blood-pressure, (4) syphilitic aortitis, (5) rupture of a valve. The physical signs are sudden, short, and forcible pulse wave, high blood-pressure, hypertrophy of the left ventricle with a diastolic murmur at the aortic cartilage, the aortic second sound being also present and indicating dilatation of the aorta. If the lesion is due to intermittent strain in an arduous occupation, mitral incompetence quickly follows, with cough, dyspnea, cyanosis, enlarged liver, fullness of the veins of the neck, edema of the legs, and death from heart-failure. Aneurism is one of the possible consequences. Uremic symptoms and angina pectoris may also be present. The prognosis is always unfavorable, sudden death being of frequent occurrence. Broadbent (Practitioner, March, 1908).

ETIOLOGY.—Aortic regurgitation is seen most often in middle-aged, vigorous men accustomed to considerable muscular exertion. Recent studies have shown that 75 per cent. at least of pure aortic cases are due to syphilis. It may also be caused by endocarditis, arteriosclerosis, the poison of gout, alcohol, etc.

Atheroma of the aorta may extend into and deteriorate the valves.

The valves may be congenitally affected. In most such cases they are still competent at birth; but they are apt to become impaired in later life.

Ulcerative endocarditis may produce a sudden incompetency of the valve, with great and perhaps fatal embarrassment of the cardiac circulation, as already mentioned. And, finally, sudden muscular strain may produce a rupture of one of the segments, especially if the valve is previously impaired by disease.

In 85 per cent. of the cases of aortic insufficiency and aneurism, as well as in cases in which mesaortitis is suspected for clinical reasons, the syphiliitc etiology can be demonstrated by means of Wassermann's reaction, even when historic data and all the characteristic symptoms of syphilis are absent, while the reaction is negative in cases of pure arteriosclerosis. Donath (Berl. klin. Woch., Nov. 8, 1909).

Twenty-one cases of aortic endocarditis associated with that type of mesaortitis which is considered to be of syphilitic origin. All but 3 of these cases presented definite signs of aortic insufficiency during life. Seventeen of the patients were under 50 years of age, and in 11 a definite history of syphilis was obtained, or gummas were found at autopsy. A history of rheumatic fever was conspicuous by its absence. In 76 other cases of chronic aortic endocarditis, 21, which showed lesions of other valves as well, and were for the most part almost certainly of rheumatic origin, had smooth, delicate aortas. In the other 34 cases, 66.6 per cent. of which were over 50 years of age, the chronic aortic endocarditis was in most instances associated with an arteriosclerotic process in the aorta, but not a true mesaortitis. Longcope (Jour. Amer. Med. Assoc., Jan. 8, 1910).

PATHOLOGY.—Besides the usual changes in the valves themselves, there are lesions peculiar to aortic regurgitation in the heart and blood-vessels. As already stated, the heart becomes enormously hypertrophied, weighing 40 to 45 ounces instead of 10 or 12. The main part of this increase is in the walls of the left ventricle, the cavity of which is enlarged, but its walls more than proportionately thickened. The muscular trabeculæ of the ventricle are usually more or less flattened where the regurgitant blood-current impinges upon them.

While in all kinds of valvular lesions the heart is exposed to ultimate degenerative changes, this liability is particularly great in aortic regurgitation, because the coronary arteries upon which the nutrition of the heart wall depends, originating, as they do, at the base of the semilunar valves, no longer have a normal amount of blood forced into them. Moreover, if the lesion of the valves is due to fibrotic changes, the orifices of the coronary arteries are apt to be involved in this process and more or less occluded. Hence those cases of aortic regurgitation have a decidedly better prognosis which are due to rheumatism than those which are associated with atheroma.

The systemic arteries become dilated by the large volume of blood which is thrown into them with each contraction of the enormous left ventricle, and they also undergo sclerotic degeneration because of the strain which they experience.

PROGNOSIS.—Aortic regurgitation is the most dangerous of the acquired valvular lesions of the heart. It is consistent with comfort and vigor lasting for years, but there is always the possibility of a sudden fatal termination; and when once compensation has been interrupted, it is seldom satisfactorily restored. Sometimes upon the development of secondary mitral insufficiency there will be a noticeable alleviation of the cardiac embarrassment, but the patient is reprieved, not saved.

Pure aortic stenosis is not very common, but is more frequently met with in combination with aortic regurgitation, when the modification in the character of the pulse which it entails is of great diagnostic value. It is one of the least serious of the valvular lesions unless associated with degenerative changes in the aorta in later life. It is not progressive in the same degree as mitral stenosis.

The prognosis in mitral stenosis is always serious as regards duration of life, though the patient may survive a considerable number of years, as the tendency is for the constriction of the mitral orifice to be progressive. Broadbent (Dublin Jour. of Med. Sci., April, 1909).

TREATMENT.—When the aortic valves are diseased from causes other than endocarditis, **iodide of potassium** in doses of 5 to 10 grains thrice daily given for long periods has been followed by great improvement. This is no doubt due to the fact that so many of these cases are syphilitic in origin. They should always be investigated with this point in mind, and, if found to be syphilitic, should be given vigorous antisyphilitic treatment. This applies to cases of stenosis as well as regurgitation.

Some writers have advised against the use of **digitalis** in aortic insufficiency, fearing the bad effect of lengthening the diastole and thus affording a longer time for regurgitation; but the weight of authority is undoubtedly in favor of employing digitalis when it seems to be needed, despite this theoretical objection.

> By far the most important time for treatment is at the onset in rheumatic cases. Children with growing pains or a pain in any joint should always have their hearts examined—the onset of endocarditis is so insidious. During the acute stage **salicin** or **aspirin** given in full doses appears to be less depressing to the heart than salicylates. Small repeated **blisters** to the first, second, or third spaces on the left side, as recommended by Caton, are distinctly useful, as also is **potassium iodide** after the temperature has fallen. When the aortic valve is affected, **rest** in bed is essential, not only until the temperature comes down to normal, but for at least six weeks after, and then a very gradual return to being up all day, and no exercise or work should be allowed for six months or more. If so treated the murmur and all signs of the regurgitation will in rare instances completely disappear. This happened in a recent case under the writer's observation. But when the regurgitation persists, as it usually does, compensation is attained with as little dilatation as possible, and so more reserve is left for future contingencies.
>
> In syphilitic cases **potassium iodide** tends to prevent the increase of the lesion, and does good by lowering the vascular tension. Atheromatous cases need tonics combined with measures to reduce the peripheral resistance.
>
> In all cases tonics such as **strychnine, arsenic, formates, ammonia,** and bark are most useful, and **belladonna** if there is palpitation. The bowels should be kept regular, but no violent purgative must be given because of the danger of fatal syncope. Flatulent distention of the stomach should be watched for and treated, since it may bring on angina pectoris earlier than need be. Whenever there are symptoms of cardiac distress, rest in bed for two weeks to a month should be ordered, and the getting up after this must be gradual. The patient ought also to be warned of the extreme danger of any sudden exertion. Hypodermic injection of **morphine** is the best hypnotic if the nights are bad.
>
> If venous congestion or dropsy comes on, **digitalis** combined with vascular dilators and diuretics is useful until these symptoms have been got rid of. Then, if the mitral and tricuspid breakdown was due to the amount of the aortic regurgitation, the digitalis must be at once stopped, since it is a dangerous drug to use in aortic regurgitation. Bleeding is never safe, but a few **leeches** may sometimes help the digitalis when there is venous congestion. Broadbent (Lancet, Nov. 12, 1910).

Further suggestions will be found under TREATMENT OF VALVULAR DISEASES, at the end of this section, page 500.

AORTIC STENOSIS.

DEFINITION.—A lesion of the aortic valve obstructing the normal flow of blood from the left ventricle into the aorta.

SYMPTOMS.—Well-compensated aortic stenosis may last for years without subjective disturbances. When compensation begins to fail, the pulse may become very slow, even as slow as 50 to 25 beats a minute, and there is a great tendency to dizziness, faintness, syncope, and epileptiform attacks. The subjects are frequently syphilitic. In elderly persons the lesion is generally due to simple arteriosclerosis. Upon inspection, the heart's apex may be seen downward and to the left from its normal position; but in some instances, when there is pulmonary emphysema or an unyielding chest wall, no cardiac impulse can be seen or even felt.

Percussion may show some enlargement of the left ventricle. Change in the right side of the heart does not ensue until the later stages of the disease.

Palpation very often detects at the base of the heart on the right side a distinct rough, systolic thrill.

Auscultation discloses a rough, long-drawn, systolic murmur, heard best in the second right interspace, of a sawing character, and transmitted into the carotids. It is followed by the second aortic sound, unless there is also a diastolic murmur, when the latter may supplant the normal valvular sound. Often there is accentuation of the second aortic sound, particularly if there be chronic degenerative changes in the kidney.

The murmur is not invariably harsh. It may exceptionally be soft and blowing, or even musical.

DIAGNOSIS.—A systolic murmur at the base of the heart may be heard in anemia, but this is usually in young subjects, and loud upon the left as well as upon the right side of the sternum, and it is not accompanied by the characteristic thrill nor by hypertrophy of the left ventricle. A systolic aortic murmur is heard very frequently in connection with the murmur of aortic regurgitation independent of any stenosis. This murmur is comparatively soft in character and unaccompanied by thrill. A systolic murmur may be heard in the aortic region caused by roughening of a calcified aorta without the existence of stenosis. Here we would fail to find enlargement of the left ventricle, or the peculiarly slow, infrequent pulse of stenosis. The systolic bruit of a thoracic aneurism, heard in the same region, would be accompanied by pain, dilating tumor, X-ray shadow, and other signs of the true condition, and not associated with the peculiar pulse or with any hypertrophy of the left ventricle unless there were coexistent aortic regurgitation. A mediastinal new growth may press upon the aorta in such a way as to cause a harsh systolic murmur, but without any necessary sclerosis of the arteries, as seen in aortic stenosis, and with a tumor to be detected by percussion and by the X-ray. Moreover, the blood-count might aid here in diagnosis.

The systolic murmur of pulmonic obstruction and that of patent ductus arteriosus are not transmitted into the systemic arteries.

ETIOLOGY.—In some cases the valves appear as if the lesion might have been congenital, but almost always the disease develops late in life, and is a slow, fibrous, and calcareous change in the valves associated with degenerative changes in the whole arterial system. The left ventricle is slightly dilated, but mainly hypertrophied.

PATHOLOGY.—Sometimes there is a subvalvular stenosis because of fetal endocarditis. There may be vegetations on the valves due to endocarditis. Usually the lesion is sclerotic or calcareous. The coronary arteries may be involved, resulting in myocardial degeneration.

PROGNOSIS.—The prognosis is comparatively favorable. Good health may be enjoyed for many years. When compensation begins to fail, sudden death, with cerebral symptoms, may occur.

TREATMENT.—Iodide of potassium in small doses, long continued, may be of great value.

For further suggestions the reader is referred to Treatment of Valvular Diseases, on page 500.

TRICUSPID REGURGITATION.

DEFINITION. — Insufficiency of the right auriculoventricular valve.

SYMPTOMS.—The symptoms of tricuspid regurgitation are those seen in most cases of ruptured compensation, in valvular lesions of the left side of the heart, provided the patient lives long enough. They are headache, dizziness, indigestion, scanty urine, uneasiness in the right hypochondrium, wakefulness, cyanosis, anasarca, and orthopnea. Sometimes there is a peculiar greenish coloration of the skin, due to a slight icteric hue mingling with the cyanosis.

On physical examination we find by inspection a marked epigastric impulse, and by percussion a very extensive dullness to the right of the sternum. The characteristic murmur of tricuspid regurgitation is a soft, low, systolic murmur, heard best at the left edge of the sternum between the fourth and sixth ribs, and transmitted toward the right. It is seldom audible above the third rib. The incompetency of the tricuspid valves causes dilatation of the subclavian and cervical veins, and when this has become so great that their valves are no longer competent the veins pulsate with every systole of the heart. This pulsation may be seen sometimes even in the axillary, thyroid, and mammary veins. The same systolic centrifugal impulse is also transmitted downward into the liver, and this organ may exhibit an expansile pulsation with every cardiac systole.

> Heinrich Stern, in 1910, called attention to a new posture which he found of value in detecting tricuspid regurgitation, of inducing the characteristic murmur of this disease when it has been absent, and making it more distinct when it is vague and indistinct. When a patient is in the recumbent posture, if the head is lowered, the jugular veins become distended, and as a rule begin to pulsate. If the head is lowered beyond a certain degree, the pulsation and engorgement recede. This lowering of the head stretches the muscles of the head and also the jugular veins. This stretching is reflected in the tricuspid area, and murmurs are now evident which were not heard before, or which were quite indistinct. The apex beat becomes more pronounced and any other accompanying murmurs are more audible than when the patient was in the ordinary recumbent position. In Stern's posture a tricuspid murmur once heard is always heard. The venous hepatic pulse, a characteristic phenomenon of tricuspid insufficiency, is more easily observed in this posture. Sachs (Med. Record, Feb. 10, 1912).

DIAGNOSIS.—The systolic murmur of mitral regurgitation is heard upon the left side of the sternum; as a rule, loudest at the apex, and transmitted toward the left axilla. If both the mitral and the tricuspid valves are incompetent, usually upon careful use of the stethoscope an area can be found, going from left to right, where the mitral systolic murmur ceases, and on farther advance toward the right an area where the tricuspid murmur begins. Moreover, the latter murmur may be different in pitch and quality from the mitral murmur.

> In a certain number of cases, it is possible to exclude tricuspid insufficiency, notwithstanding the existence of the jugular-ventricle pulse. These are the cases in which the jugular pulse is so weak that it is scarcely recognized as such, but the pulse is of the permanently irregular type, there are no signs of stasis and there may be absolutely no heart murmur. These features of the case exclude tricuspid insufficiency. Only when the jugular-ventricle pulse is pronounced should it be suspected. Hering (Med. Klinik, Sept. 19, 1909).

ETIOLOGY.—Tricuspid incompetency is usually secondary to dilatation of the right ventricle because of obstruction in the pulmonary circuit. This may be due to chronic bronchitis, pulmonary emphysema, fibroid induration of the lungs, or to mitral disease. Of these two classes of causes, the pulmonary are said to be of more unfavorable prognosis. Also, tricuspid regurgitation may be directly due to endocarditis. This may exceptionally affect primarily and alone the tricuspid valve, but it is mostly secondary to trouble upon the left side of the heart. If the endocarditis is ulcerative, there may be secondary pulmonary abscesses.

TRICUSPID STENOSIS.—Tricuspid stenosis is an extremely rare condition, causing obstruction of the right auriculoventricular valve. It may be congenital, in which case it is associated with other lesions, so that the patient seldom lives long. If acquired, it is almost invariably associated with other valvular lesions, particularly mitral stenosis.

Its symptoms are cyanosis, sensitiveness to cold, dyspnea, and palpitation. A presystolic thrill has been observed, and a presystolic murmur, heard best at the base of the xiphoid cartilage or toward the right from that point.

> The diagnosis of tricuspid stenosis is very difficult. In a table of 117 cases, by Lendet, it was made out during life only 6 times. The lesion is almost always combined with mitral stenosis, and both usually result from rheumatism. The patients are mostly females and rarely more than 40 years old. With the usual signs of mitral stenosis are associated, when combined with the tricuspid lesion, a feeble thrill and murmur over the sternum. The enlarged auricle is also likely to be notably enlarged, and before the heart breaks down there is likely to be subcutaneous dropsy, turgidity of the jugular veins, cyanosis, and dyspnea. The prognosis is very bad in congenital cases, children seldom exceeding the fourth or fifth year. In the acquired disease the average duration of life is 35 years. Crawford (Pract., Feb., 1907).
>
> Stenosis of the tricuspid orifice can hardly ever be recognized by the usual clinical means of investigation; when graphic methods are employed its presence can be determined positively. In reference to his case, the points to be noted are: The tracings obtained proved conclusively the presence of a tricuspid stenosis. Most likely there was also a mitral lesion, because of the systolic murmur transmitted to the left and the extensive enlargement of the heart to the left. Felberbaum (Med. Rec., Aug. 28, 1909).
>
> Tricuspid stenosis is often due to endocarditis following rheumatism, or some other acute infection. The fact that it is almost invariably accompanied by lesions of the mitral or aortic valves confirms this view. Osler states that congenital cases are not uncommon; they are usually accompanied by some

other defect. But there are also cases of congenital origin. These congenitally defective valves are undoubtedly very liable to postnatal endocarditis. The conspicuous symptom is the extreme cyanosis in the majority of cases. This is due to the marked venous stasis resulting from the tricuspid narrowing. Occasionally it has been absent. Otherwise, there is nothing characteristic. Dyspnea may be extreme when broken compensation, due to overdilatation of right auricle, supervenes. It is surprising with what degree of comfort these patients are enabled to go about for years. T. B. Futcher (Amer. Jour. Med. Sci., Nov., 1911).

The etiology and pathology are not different from those of the more common valvular lesions.

The prognosis is very unfavorable.

TREATMENT.—This is important in the sense that the prognosis will depend upon the severity of the back pressure and the power of response to measures of relief. These measures should aim more at the relief of resistance than at increasing the power of the heart. The heart needs soothing and rest, and if these are obtained relief for a considerable period may result.

PULMONARY STENOSIS.

DEFINITION. — Obstruction of the pulmonary valve.

SYMPTOMS.—This condition is almost invariably congenital, and it is usually associated with other structural anomalies, such as persistence of the foramen ovale and of the ductus Botalli, and defects in the septum ventriculorum. Most cases come to an early termination. Life is seldom prolonged beyond fifteen years. The marked symptoms are cyanosis, dyspnea, clubbing of the ends of the fingers, and deficient bodily development.

Upon auscultation we hear a loud systolic murmur over a rather extensive area, but loudest in the second left interspace, and sometimes accompanied with a systolic thrill. The pulmonary second sound is weak or absent, or it may be replaced by a diastolic murmur. The systolic murmur is not transmitted into the arteries of the neck, but in some cases seems to extend toward the left shoulder.

DIAGNOSIS.—It should be borne in mind that functional systolic murmurs may be heard in the second left interspace. They can be distinguished by the other physical signs and the age and general appearance of the patient. And it should also be remembered that sometimes the murmur of mitral regurgitation may be heard along the left edge of the sternum; but the latter murmur may also be heard in its usual position near the apex or in the back near the angle of the scapula. Moreover, the general symptom-complex would doubtless aid in distinguishing the true lesion.

In 3 cases reported by the writer mitral lesion so raised the pulmonary artery blood-pressure that that vessel and along with it the pulmonary orifice dilated and a murmur occurred, which appeared periodically in 2 of them over a period of years. These 3 cases are examples of the so-called Graham-Steell murmur. In 2 other cases cited no such cause seemed to exist, and probably the leakage was more due to relaxed tissues about the pulmonary orifice than to any marked increase in the blood-pressure of the pulmonary artery. A pulmonary systolic murmur, the commonest of all functional bruits, probably depends on a dilatation of the pulmonary artery, and in most cases tends to disappear. When, however, the dilatation involves the pulmonary orifice so that a diastolic leakage occurs the condition is of more import, although even yet it may completely clear up. Rudolf (Amer. Jour. of Med. Sci., Sept., 1911).

ETIOLOGY.—Acquired pulmonary stenosis is rarely met with; the few instances on record being ascribed to acute rheumatism, acute infective diseases, and septic states, such as puerperal fever. Practically all cases, as previously stated, are congenital.

PROGNOSIS.—The prognosis is always unfavorable. Besides the impending cardiac failure, such patients are notably predisposed to pulmonary tuberculosis.

TREATMENT.—As to treatment, bronchial catarrh must be avoided, a dry and warm climate must be selected, and great exertion must be avoided. In general, the treatment must be symptomatic, on the lines applicable to cardiac failure, all indications for which are given below.

PULMONARY REGURGITATION.

Pulmonary regurgitation is deemed an excessively rare valvular lesion which is said to be accompanied by a diastolic murmur heard best over the pulmonary area, and transmitted downward and toward the xiphoid cartilage. It is usually associated with pulmonary stenosis or with some lesion on the left side of the heart. As distinguished from aortic regurgitation, it does not present the arterial and capillary symptoms of that disease, nor the striking hypertrophy of the left ventricle.

High pressure in the pulmonary artery may give rise to a functional leak in the pulmonary valves (Graham Steel, Barr, Gibson, and others). For instance, this may be heard in some examples of mitral stenosis. In this case we have the picture of the principal organic lesion to show us the proper diagnosis.

Pulmonary regurgitation is the rarest of all heart lesions, and one which is not often detected during life. It may originate in disease or defect of the valves themselves, or in dilatation of the pulmonary orifice, and of the artery as well, without abnormality of the valves. It may be either structural or functional, the latter being more frequent than the former. It is more frequently associated with mitral stenosis than with any other heart lesion. It is also associated with emphysema. The condition is subsequent to the dilatation of the infundibulum of the right ventricle. There are no indications for treatment of pulmonary regurgitation different from those which are applicable to valvular disease in general. Crawford (Practitioner, Oct., 1907).

TREATMENT OF VALVULAR DISEASES.—Our first effort must be to promote and maintain perfect compensation of the valvular lesions. Our most important means to this end is control of the diet and of the bodily and mental activities. The **diet** should be **simple, nutritious,** easily digested, and the amount taken at any one time should be moderate. A considerable proportion of nitrogenous elements is desirable; sugar and starchy foods should be used sparingly. Thirst should mainly be quenched with pure water; this, again, is better taken frequently in moderate amounts than in excessive draughts. Tea is to be forbidden. Coffee may be enjoyed in moderate quantity if its effects do not prove unfavorable. Cocoa, milk, soups, and broths are suitable elements of the diet. In elderly and feeble persons, and in those previously habituated to its use, a moderate amount of alcohol may be advantageous; but, in general, its daily employment is harmful. Mental strain, overwork, worry, and excitement, even if pleasurable, shorten the prognosis of comfortable existence. Physical exercise should not be summarily interdicted; its kind and amount should be most carefully determined in each individual case, and—above all—its effects alertly observed for future guidance. The **moderate employment** of many **muscles** is, of course, much better than the undertaking of special feats of strength. Walking and horseback-riding are suitable. Golf can be recommended for many patients with moderate lesions. The bicycle, if used, should be of low gear, and the patient should be warned against long journeys and against mounting hills. Facing a high wind has proved harmful, and even fatal, to cardiac patients. When ordinary exercise is no longer wise, **massage** and **passive movements** may be of great benefit; also **stimulating baths,** as those of Nauheim. Many patients are anemic, and are benefited by **iron,** and others by **arsenic**; but this latter drug should not be used where there is any suspicion of tendency to fatty degeneration. Cases which evince a liability to pulmonary disturbance (especially mitral diseases) should be guarded against exposure to cold and wet.

If sudden cardiac failure develops, particularly in mitral cases, the **abstraction** of 10 or 20 ounces **of blood** from a vein may save life. If the symptoms are less urgent, analogous relief may be obtained by a **purge,** in which case **calomel** seems particularly efficacious.

In *mitral regurgitation* and also in *tricuspid regurgitation,* two main lines of treatment are indicated, viz., to diminish the resistance in the vessels and to increase the power of the heart. **Rest** is the first and most essential agent, and alone will often suffice to restore equilibrium; it should be complete and in bed, and should be relaxed only as improvement becomes marked. The most valuable auxiliary of rest is **digitalis,** which acts as powerfully on the right ventricle as on the left. It should be given at first in small and gradually increasing doses, so as to give the pulmonary circulation time to readjust itself to the increased driving power of the right ventricle; not a few instances of hemoptysis have resulted from disregard of this condition. In grave cases it should be given with the usual precautions, viz., after a free **initial purge** to unload the veins, and combined with more rapidly acting stimulants, such as **strychnine, ammonia,** or **ether,** to tide over the delay of its effective doses. **Calomel** is probably the best purgative to employ, as it seems to be diuretic in conditions of cardiac back-pressure. As a rule, with rest and digitalis, in a few days the circulation is steadied, free diuresis set up, and dropsy begins to disappear. At the same time the murmur and systolic venous pulse may vanish. At times diuresis fails, or is inadequate; then **theobromine** or **caffeine** may be given with **salicylate of soda.** When the whole body, and perhaps the serous sacs as well, is dropsical, these measures are all apt to be quite ineffectual, until such effusion has been relieved or removed; then **paracentesis** of the abdomen or thorax, or **puncture** or **incision** of the feet and legs, may be a necessary prelude to the success of digitalis. Such relief is usually followed by a rapid increase in the output of the urine, and by a return of restful and comfortable sleep.

There are cases, commonly those in which dropsy is not prominent, in which the strain on the right heart is so great that the patient is livid and on the verge of suffocation; then **early venesection,** followed by diffusible stimulants, such as **ammonia** and **ether,** offers the best chance. Acute distress of this kind in tricuspid regurgitation is nearly always attended by two dangerous auxiliaries, sleeplessness and vomiting, directly due, in each case, to venous stagnation. Sleep must be obtained, and at times at any price. **Morphine** may be given most safely in the form of suppository, but if given subcutaneously it may be advantageously combined with **strychnine.** Crawford (Practitioner, June, 1907).

When the signs of failing compensation are more gradual, our best remedy is complete **rest in bed.** A fortnight or two thus spent may fully restore compensation, independently of any drugs.

The treatment of *mitral stenosis* in childhood is mainly the treatment of rheumatism. The parents should be warned of the meaning of sore throats, fleeting pains, nervousness and chorea, feverishness and pallor. If possible such children should be taken from damp, low-lying houses, and properly clothed and their extremities protected. Large unhealthy tonsils should be enucleated. Spring and autumn, and particularly sudden damp cold after much heat, should be a signal for added watchfulness. Early symptoms should be promptly treated by **rest** and **warmth** and the use of **salicylate of soda.** F. J. Poynton (Clin. Jour., July 21, 1909).

In *mitral stenosis* it is not necessary to employ any medication having a special action on the heart and circulatory system, so long as compensation is fairly good and the central organ is doing its work efficiently. It is when the heart is flagging that special treatment is called for. A long **rest in bed,** say for a month, will often restore a laboring heart to an efficient discharge of its work. But the time comes, sooner or later, when compensation fails, and more energetic measures are called for. Rest in bed is again one of the best aids to recovery. In the earlier stages of cardiac failure, the freshly made infusion of **digitalis** is the most reliable, given in full doses for three or four days, while the patient is resting in bed.

Convallaria majalis has certain advantages, in that it has no cumulative effect, and does not so readily produce nausea as does digitalis. It is well to commence with small doses (10 minims —0.6 c.c.) of the tincture. **Strophanthus** in the form of tincture may be prescribed in doses equal to those of the tincture of digitalis. It is especially valuable as a cardiac stimulant before edema has commenced.

There comes a time when the heart ceases to respond to any of these remedies when used singly. Then **all** three, **digitalis, convallaria majalis,** and **strophanthus,** are **combined,** and give remarkable results.

When stenotic patients have hemorrhage from the lungs, nothing should be done to arrest it provided it is not excessive. It is evidence that the patient ought to have been treated by **bloodletting.** Many cases regarded as acute edema of the lung are really cases of pulmonary engorgement due to mitral stenosis. The writer has 2 patients under observation who are bled, from time to time, with marked benefit. It is a form of treatment which need not, and should not, be delayed until an advanced stage of the disease has been reached. It should not be adopted as soon as congestion of the bases of the lungs and signs of engorgement of the liver have been detected. Taylor (Practitioner, Aug., 1912).

In cases which have advanced still farther downward, either in spite of or before our ministrations, the treatment becomes the same as that indicated in dilatation. Briefly, this consists of absolute **rest** in bed, or if he cannot lie horizontally, in a chair. The **diet** should be bland but include viands, eggs, fowl, and gruel. Alcohol and wines should be kept for emergencies. Laxatives and even purges are very helpful, acting sometimes like venesection, in relieving engorgement. **Blue mass** or **calomel** followed the next day by a saline prove most satisfactory. Equal parts of **potassium bitartrate** and **jalap powder 1 to 2 tea-**

spoonfuls are also effective. To sustain the heart, our best stimulant is **digitalis.** This is indicated only when the heart's action is feeble and ineffective, particularly if rapid and irregular. A complete study of the therapeutics of digitalis and particularly in its relation to valvular disorders will be found on page 109 of the present volume.

If there is considerable dropsy, **digitalis** will work to much better advantage if **preceded** by **free purgation** with **calomel, blue mass,** or a concentrated solution of **sulphate of magnesia.** The mercurials seem to possess a peculiar power of dilating the arterioles, which other purgatives do not have. Digitalis is much more effective if great bodily quiet is enforced during its administration. If given at all, its dose should be such as experience finds suitable in the particular case in hand. If an ordinary dose does not seem to be of much benefit, gradually increasing amounts should be given until either there is improvement in the pulse or some toxic effect appears.

Nausea and diminution in the amount of urine are signs that digitalis had better be omitted. Some excellent observers believe that better results can be obtained from the use of the **digitalis** leaves, or an **infusion** made from them, than from the tincture. An easy way to obtain a fresh infusion for the patient is to order powders of digitalis, each one of sufficient size to make an infusion for twenty-four hours' use. No alkaloid of this drug appears to represent all its beneficent powers. In some instances, where there was obstinate vomiting, **digitalis** has been given with advantage **by enema.** When the heart appears to have come under its influence, we must be prepared to interrupt its administration as soon as there is any diminution in the secretion of urine or tendency to nausea or to a fresh irregularity of the pulse.

If digitalis, after a careful and persistent trial, proves unavailing, recourse may be had to tincture of **strophanthus, caffeine, sparteine, adonidin,** or **convallaria majalis;** but, unfortunately, these are seldom of great advantage. **Strychnine** is a valuable, general, and cardiac tonic. It may be used to supplement other treatment, and also subcutaneously in case of dangerous collapse.

Nitroglycerin will often give great relief to cardiac distress and to dyspnea, particularly where the pulse is hard or where there is cyanosis.

In aortic regurgitation the following treatment is recommended: In cases severe enough to be admitted to hospital, **rest** often over a long time is necessary. **Restriction** of the amount **of fluid** taken, so far as can be done without discomfort to the patient, is valuable, by relieving the work of the heart by after a time diminishing the amount of fluid in circulation. In the absence of rheumatic manifestations or of fever, the writer has not seen much benefit from the continued use of the salicylate group of drugs; short courses may be useful in relieving precordial pains. **Digitalis** was given whenever there were signs of heart-failure according to the indications in each individual case as they occurred from time to time; it is more often necessary than in the aortic disease of adults partly because of the far greater frequency of implication of the mitral valve. As to relief of special symptoms, the most urgent are the very distressing and sometimes alarming attacks of angina pectoris, which are not infreqent. In young patients **amyl nitrite** is the most effectual drug. In several cases, **nitroglycerin,** and the other **nitrites,** com-

> pletely failed both to relieve and prevent the attacks, when amyl nitrite gave prompt relief, but, of course, did not prevent their recurrence. The dose inhaled has sometimes to be increased up to ♏x to ♏xij (0.6 to 0.75 c.c.) at a time to maintain the effect, but seems to entail no unfavorable consequence. The next most urgent symptom is the attack of dyspnea or suffocation, which is probably a form of angina. Here again **amyl nitrite** often relieves, but sometimes **caffeine** and **ammonia** is more effectual. Not so immediately urgent, but distressing from its persistence, is the excessive or violent pulsation of the greatly enlarged heart. This palpitation is often the subject of the patient's chief complaint. The writer has found a mixture of **Fowler's solution, dilute hydrocyanic acid,** and tincture of **veratrum viride,** given for some time, most useful in the treatment of this symptom, which is often a most troublesome one, even when the patient is at rest in bed, and when there is no evidence that the heart is not able, in spite of the abnormal conditions, to maintain an efficient circulation. Clarke (Brit. Med. Jour., June 10, 1911).
>
> In aortic stenosis and insufficiency **thiosinamine** often gives some relief from dyspnea, though auscultatory signs unmodified. A daily dosage of 0.06 to 0.1 Gm. (1 to 1½ grains) by injection or ingestion can be safely employed. Rénon (Bull. de l'Acad. de Méd., April 25, 1911).

In case of marked dropsy **diuretin** will sometimes prove very valuable. Another suitable remedy is a pill composed of 1 grain each of **squill, digitalis,** and **blue mass,** administered three times a day. If the kidneys are practically intact, **calomel** may be administered as a diuretic in the dose of 3 grains every three hours until effect: either decided purging or marked diuresis. The likelihood of purging may be diminished by combining, with this dose of calomel, opium in the amount of ½ to 1 grain. In case there is a considerable collection of fluid in one or more of the serous cavities of the body, **aspiration** may give great temporary relief and enable the heart to recover some of its lost power; and when the legs are extremely edematous, the use of **Southey's tubes** or **scarifications** under strictly antiseptic precautions may be of great advantage.

Herman F. Vickery,
Boston.

ENDOMETRITIS.—DEFINITION.—Endometritis is an inflammation or hyperplasia of the uterine mucous membrane involving, to a greater or less extent, the parenchyma of the uterus.

VARIETIES.—Both in a clinical and a pathological sense, it is convenient to divide the disease into two varieties, viz.: (1) *interstitial* or septic endometritis, and (2) *glandular* or functional endometritis, or hyperplasia. Either of these two varieties may exist in the *acute* and *chronic* form, but the chronic form may follow a mild and overlooked acute attack, or may supervene in a gradual manner without being preceded by a recognizable acute attack.

> The writer concludes that the classification of endometritis should be *acute* and *chronic*. Further subdivision leads to much confusion and does not materially aid the clinician. Uncomplicated cases are not very common and an uncomplicated chronic case is a very rare condition. Normally, the endometrium is free from bacteria. Treatment of chronic endometritis, to be successful, should always be carried on in conjunction with the treatment of associated conditions. Mundell (Amer. Jour. of Obstet., April, 1909).
>
> Etiologically endometritis may be divided into (1) bacterial, (2) toxic (due to chemical substances, necrotic

tissue, toxins of infectious diseases, etc.), (3) mechanical and thermal. Since, however, all these causes produce identical conditions in the endometrium, a different classification is necessary for practical purposes. The most satisfactory from this point of view is that into (1) *acute,* (2) *chronic,* and (3) *specific.* Albrecht (Monats. f. Geb. u. Gyn., Bd. xxiv, S. 397, 1911).

SYMPTOMS.—The symptoms may be divided into (1) disturbances of the sexual functions, (2) intermenstrual discharges, (3) pain and discomfort in and about the uterus or radiating from the uterus, (4) reflex disturbances, and (5) general symptoms.

Menorrhagia is one of the most frequent symptoms in the early stages, and in the *glandular* variety it often persists for a long time as the most prominent one. The flow may be moderately increased in amount or be a profuse hemorrhage with the passage of clots; it may be prolonged or may recur too often. In the later stages of *septic* or *interstitial* endometritis the menses are sometimes scanty. In certain acute attacks the menstrual flow is suppressed.

Dysmenorrhea is common in cases connected with flexion, puerile cervix, or inflammation of the appendages.

Dyspareunia and sterility may be present under the same conditions.

Leucorrhea is usually noticeable in the glandular variety and in the early stages of the septic. In the forme- the corpus secretes a thin, and the cervix a thick, clear mucus, both of which may be transformed into minute white coagula, at the external os, by the acid vaginal secretion, and appear at the vulva as a white or greenish-white discharge. In some cases the corporeal mucus is intermittingly tinged with blood. The leucorrhea may last throughout the month or only for a few days after the cessation of the monthly flow. In the septic variety the discharge is at first purulent, but later becomes mucopurulent. In cases of long standing cervical mucus may become exceedingly viscid when it is retained in the enlarged cervical glands, and gathers into a large, tenaciously adherent lump or plug at the external os. It sometimes has a disagreeable odor when it reaches the vulva.

Pain may be felt in the sacral or lumbar region, and may extend across the back or up the spine to the occipital region, or down the course of the sciatic nerve. Cutting or cramping pains across the lower abdomen or pubic region may be complained of, depending upon painful uterine contractions due to the expulsion or attempted expulsion of uterine discharges. Irritability of the bladder or rectum, or pain in the vagina or pubic bones, may be prominent. Feelings of weight in the vagina, and sensations as of prolapse of the pelvic organs are present in some cases. Intercostal neuralgia is not uncommon.

Menstrual pain of a burning or aching character may be felt in the pelvis and back, or the pain may be suprapubic and colicky. It may last one or more days or throughout the period, and even for several days afterward. When the mucous membrane is exfoliated the uterine contractions are frequent and excessively painful, and last until the membrane is expelled.

Gaseous distention of the intestines, constipation, impaired digestion

—with its accompanying reflexes, photophobia, and pain in the eyes after prolonged attempts at reading—are the ordinary reflex disturbances. Mental depression, worry, and the various manifestations of hysteria and neurasthenia are sometimes classed among the reflexes, although they are, as a rule, largely dependent upon other conditions and circumstances.

Chills, fever, and the other general symptoms of inflammation and sepsis are observed in acute endometritis.

In chronic cases anemia and nervous debility are often present, and seem to favor the development of reflex symptoms.

DIAGNOSIS.—Endometritis must be differentiated from angioma, tuberculosis, carcinoma, and myoma of the uterine mucous membrane.

Besides the symptoms, tenderness of the uterus, as evidenced by bimanual palpation, and sensitiveness of the endometrium at the internal os and fundus, as demonstrated by the passage of the sound, are of diagnostic value. The withdrawal of the sound may be followed by a slight flow of blood or mucus.

> The pronounced tenderness of the endometrium on the touch of the sound is characteristic of painful endometritis. As a rule, only certain localities (fundus and tubal insertions) give rise to the attacks of pain. The use of the **curette** brought recovery; a glandular hyperplasia could generally be found in the *débris.* Pinkuss (Monats. f. Geb. u. Gyn., Bd. xi, S. 908, 1900).

It is difficult to distinguish **angioma** from hemorrhagic glandular endometritis, except by the aid of the curette, which, in the latter case, will bring out some of the hyperplastic mucous membrane.

In **tuberculosis** of the endometrium the curette will find necrotic, cheesy particles, and, perhaps, tuberculous tissue. An accompanying bilateral salpingitis and pelvic peritonitis with encysted ascites, particularly in virgins, indicate the condition. Tuberculosis elsewhere and a slowly progressive anemia add probability.

In **carcinoma** and **sarcoma** watery discharges, fetor; gradually increasing, intermittent metrorrhagia; rapid progress, and the microscopic examination of the findings of the curette are diagnostic. Carcinomatous infiltration of the cervix produces a globular enlargement that affects the supravaginal portion as much or more than the vaginal. Carcinomatous ulceration is excavated, fissured, pale red or grayish, with vascular spots that are friable and bleed easily upon being touched. A tenaculum tears it easily and causes abundant hemorrhage, but will hold firmly in an inflamed cervix. When there is cystic degeneration the tenaculum may tear out easily, but it causes a flow of mucus from the lacerated follicles with or without some hemorrhage. The inflamed cervix is usually soft and elastic; the carcinomatous, either hard or friable. Carcinomatous ulceration of the cervical cavity is excavated, dark or dull gray in color, bleeds slightly when touched, and conveys a slight odor to the cotton with which it is wiped.

Small intra-uterine and submucous **myomata** usually cause marked enlargement of the uterine cavity, and can sometimes be felt by the sound. Digital examination of the endometrium through the dilated and incised cervix is of great value in discovering this, as also other conditions, although the procedure is only advisable in rare instances.

> The diagnosis "endometritis" should only be made when all the complex of tissue changes associated with inflammation are present; all the hyperplastic conditions without inflammation, formerly described as "endometritis glandularis hyperplastica," are to be considered as pure hypertrophies. They have nothing to do with inflammation, but the symptoms of both may be practically identical. Albrecht (Monats. f. Geb. u. Gyn., Bd. xxiv, S. 397, 1911).

ETIOLOGY.—*Acute glandular* endometritis may result from trauma or taking cold during the menstrual congestion, such as suppression of menstruation from exposure to cold, excessive coitus, overexertion, or blows upon the lower abdomen during menstruation. Poisons, such as phosphorus and the essential oils, are occasional causes.

Acute interstitial endometritis is caused by infection, such as inoculation by gonorrheal pus during or following coitus, infection of retained secundines, or the extension of sepsis from vaginal inflammation. It may also follow traumatism with immediate or subsequent infection, such as lacerations of the cervix during labor or by instrumental dilatation, curettage of the endometrium, the introduction into the uterus of strong irritants, the use of intrauterine stem pessaries or poorly fitting vaginal pessaries, irritating and unclean tampons, etc.

> Repeated examinations of the cast from a case of membranous dysmenorrhea showed numerous fresh venous thrombi in the uterine mucosa, similar to the thrombi found in the decidua in cases of premature separation of the placenta. Curetting and caustics were not curative, but **cardiac tonics, gymnastics, diet, baths,** brought about recovery. Gottschalk (Deut. med. Woch., Nov. 26, 1903).

Traumatism or reinfection may convert a chronic into an acute endometritis.

Chronic glandular endometritis may be caused by interference with the menstrual function by taking cold, overexertion, excessive coitus, laborious or sedentary occupations, uterine displacements, obstinate constipation, etc. The same causes may act during puerperal involution or after abortion. Excessive coitus, masturbation, ovaritis, uterine fibroids, inflammation in neighboring pelvic organs, and interference with uterine drainage by stenosis may lead to it.

Acute attacks and the above-mentioned causes increase the hyperemia and evolutionary changes of the endometrium that prepare it for the formation of the decidua, and disturb the involution that normally follows each menstruation. Hence, glandular endometritis differs at first but little from a subinvolution of the endometrium, and is not an inflammation according to the ordinary acceptance of the term.

Chronic interstitial inflammation may result from one or more acute attacks or from infection by objects introduced into the vagina or uterine cavity, whether by operation, examination, or improper attempts at medication.

PATHOLOGY. — The mucous membrane of the cervical cavity presents the same changes as those of other mucous membranes.

The alkaline mucous discharge that hangs from the cervix, together with the congestion and infiltration, often produces an exfoliation of the epithelium about the external os, with reproduction in the form of immature cylindrical epithelium. This condition is called *simple erosion.* The infiltration and swelling of the submucous tissues cause more or less of a rolling out, or eversion, of the mucous membrane of the cervical cavity, which is more pronounced on a lacerated cervix. More or less folding of the infiltrated mucous membrane may give the appearance of a papillary or granular surface, which is called *papillary erosion.* Pockets may form in these folds, and, together with the everted cervical glands, may become occluded, giving rise to a cystic condition called *follicular erosion.* These follicles may become so numerous, or one or two may become so large, that the normal cervical tissue is either displaced or replaced by them, and *cystic degeneration* results. Sometimes localized hyperplasias are present, with projection of glandular polypoid masses. This is shown in the annexed colored plate.

Polypoid endometritis occurs with relative frequency and is attended by serious and sometimes fatal consequences. It may be met with in any woman during the child-bearing epoch, and accounts for much of the otherwise inexplicable mortality which still occurs among puerperal women as the result of sepsis, more especially in private practice, in spite of the improved modern methods in the conduct of delivery now generally adopted. Polypoid decidual endometritis is the most important disease of the decidua, and is a frequent cause of abortion. It is a result of pre-existing chronic endometritis beginning prior to, or coincidentally with, pregnancy, and continued into the puerperium, during which acute processes are grafted on the chronic condition in consequence of septic infection. The most conclusive evidence, however, that polypoid endometritis usually commences prior to, or during pregnancy, is furnished by the fact that in many cases it is found to be distinctly syphilitic in origin, as evidenced by the history and microscopic appearances of cases examined. In many instances the mothers show no external signs of constitutional syphilis, thus illustrating Colles's law; but that the mother does not become actually immune and escape serious lesions in these cases is shown by the existence of syphilitic endometritis. During the past ten years the writer met with over 100 cases in private and hospital practice, and, at the lowest estimate, it will be encountered in from 3 to 5 per cent. of all pregnancies, whether ending prematurely or at full time. Nyulasy (Jour. of Obstet. and Gynec. of Brit. Empire, July, 1909).

The uterine mucous membrane above the internal os has somewhat different characteristics from those of other mucous membranes which have different functions. Its glands are simple depressions or epithelial tubules that extend to the muscular walls underneath. Instead of being imbedded in firm connective tissue as are the cervical glands, they are surrounded at their inferior extremities by muscular fibers projecting from the muscular walls, which constitute an ill-defined muscular structure called the muscularis mucosæ. In the interglandular or intertubular spaces or fluid are found delicate connective-tissue fibers, and round or oblong cells resembling lymph-cells.

When subjected to intense proonged congestion an infiltration of serum takes place, raising the epithelial surface and causing a proliferation of the epithelial cells, with enlargement, as well as wrinkling, twisting, or bending of the glandular tubules, or, in severe cases, a formation of new depressions or tubules, some of which may become closed by bending or swelling at their orifices.

Fig. 2

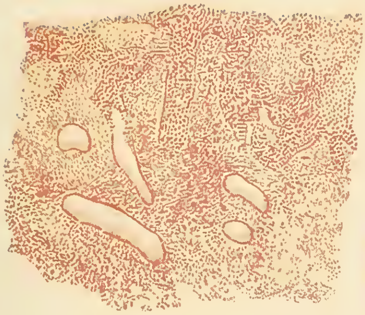


Fig. 3

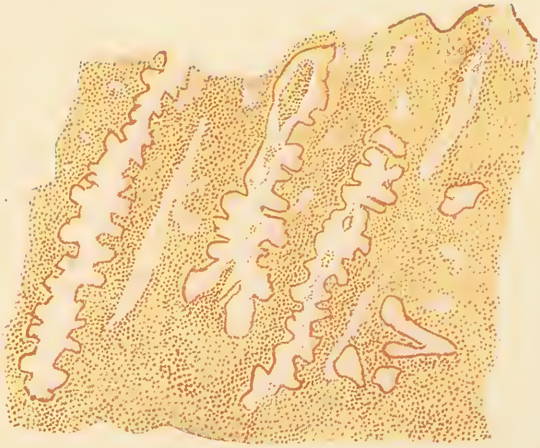


Fig. 1

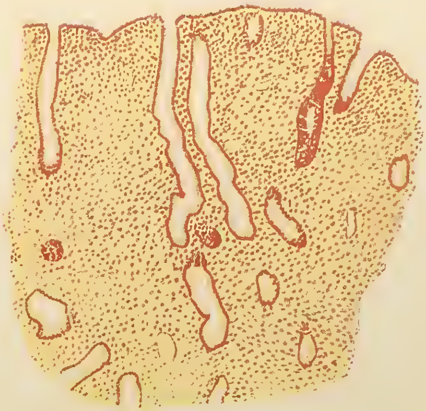


Fig. 4

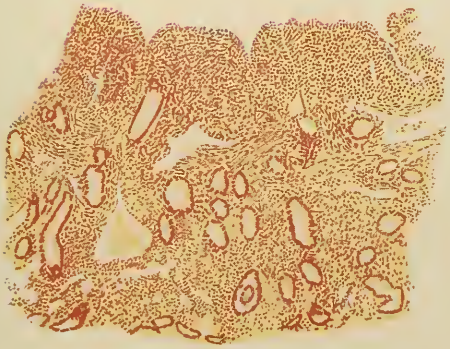
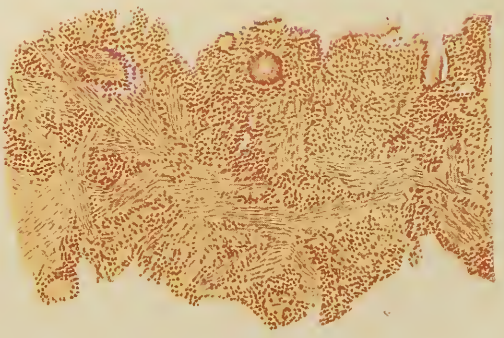


Fig. 5



Comparative Histology of Endometritis. *(Zweifel.)*

Fig. 1, normal mucous membrane. Fig. 2, beginning erosion of cervix. Fig. 3, glandular endometritis. Fig. 4, acute and chronic interstitial endometritis. Fig. 5, chronic interstitial endometritis.

In some cases the epithelium proliferates within the glands, forming more than one layer. Round-cell infiltration and formation of new interglandular tissue may take place, with proliferation of the epithelial cells within the glands so that they may form more than one layer, particularly if septic infection intervenes. In such cases agglomerations of glands surrounded by a small amount of connective tissue project from the surface, forming polypoid masses, which may spring from every part of the mucous surface.

> Decidual cells are never found in the stroma of the endometrium in the glandular forms of endometritis. Cells resembling the decidual are found in the interstitial and mixed forms of endometritis, but only in the superficial layers. These cells lie at some distance from one another among the comparatively normal cells of connective tissue. Tavilladaroff (Roussky Vratch, March 6, 1904).
>
> The most important variations recorded by various authors are as follows: (1) Endometria which show a definite cyclic stage, which, however, does not correspond to the clinical stage. (2) Endometria whose anatomical condition does correspond to the clinical stage, but which show hyperplastic processes, such as invagination or clumping of glands. (3) Endometria which show the anatomical characteristics of several different stages. (4) Endometria which, taken from the ninth to the fourteenth day, show a condition corresponding to the end of menstruation. (5) Endometria which always show one definite gland type, no matter in what period of the menstrual cycle the examination is made. The writer examined with great care the endometrium from 205 patients, in all of whom the exact date of the preceding menstruation, and the menstrual type, was known. The specimens were obtained in part from extirpated uteri, in part by curettage. In 120 of these cases, or 66 per cent., the anatomical picture presented by the endometrium corresponded with the clinical stage at which it was removed; in 22 cases the endometrium presented a uniform anatomical picture, but this corresponded either to an earlier or a later stage than that actually presented by the patient. In all the remaining cases the structure of the endometrium showed variations from the normal, and these have been therefore classed as "pathological" (entirely irrespective of the presence or absence of inflammatory changes). Schröder (Arch. f. Gyn., Bd. xcviii, S. 81, 1912).

The uterine walls are usually also congested, and some round-cell infiltration takes place about the blood-vessels, which, in time, leads to the formation of adult connective tissue. Contraction in this connective tissue may finally cause anemia of the uterine walls and more or less atrophy of the muscular fibers.

The mucous membrane is hyperemic, softened, thickened, and dark red in color. In places it may have a mottled appearance, due to minute extravasations of blood. The surface is smooth, sometimes irregular, and is moistened with a thin, clear, grayish or pinkish mucus. The pouting mouths of the congested and enlarged glands are visible. The uterine walls are slightly thicker and the uterine cavity somewhat longer than normal (from 2½ to 3 inches deep from the external os to the fundus). This condition is that of *glandular* endometritis, or *hyperplasia* of the endometrium, and is seldom the result of infection. It is, as a rule, chronic.

> A study of the condition of the endometrium in 130 preparations showed that aside from physiological variations in the form and number of the uterine glands, there is a true glandular hyperplasia and hypertrophy. From these result abnormalities of secretion. This

must be recognized when there is a progressive process going on in the glands; when there is production of cysts and invaginations; and when we find gland forms in the premenstrual interval. Signs of importance are inflammation of the plasma cells, and changes in the spindle cells and connective-tissue cells. If we find hyperplasia and hypertrophy of the glands combined with inflammatory changes, or the remains of such changes in the stroma, there is no reason why we should not make the diagnosis of an inflammatory origin of these lesions. K. Himmelheber (Monats. f. Geb. u. Gyn., Aug., 1909).

During the menstrual periods the congestion is intense, and there is more or less extravasation of blood in the interglandular spaces, leading to extensive exfoliation of the epithelium, and detachment of portions of the mucous membrane.

When the uterus is curetted for supposed endometritis, much that is taken for endometritis is in reality nothing more than the natural premenstrual congestion. In some cases, glandular changes are really pathological, and have nothing to do with menstrual congestion. In other cases, the mucosa may be chronically congested in consequence of displacement of the uterus or of inflammation in the adnexa, or is primarily affected. Chronic congestion in the uterus from inflammation in the adnexa leads to overnourishment of the glands and they become hypertrophied and functionate to excess, increasing the discharge, which thus is one of the most constant signs of endometritis. The menstrual flow comes on earlier and lasts longer than normally and may become irregular. Schickle (Beiträge z. Geburts. u. Gynäk., Bd. xiii, Nu. 3, 1909).

Endometritis represents pathological changes which are entirely dependant upon the time relation of the menstruation and not upon inflammatory processes. If the curettings, therefore, are derived from a uterus just before menstruation, the picture of the so-called "hypertrophic" endometritis will present; while curettings from the postmenstrual period will show all the typical changes of "atrophic" endometritis. C. C. Norris and F. E. Keene (Surg., Gynec., and Obstet., Jan., 1910).

Writers undertaking to describe the pathological changes have constantly confused them too much with the physiological changes that take place during the menstrual cycle. Before attempting to recognize the results of infection in the endometrium it is absolutely necessary for one to familiarize one's self with the scattered round cells and groups of lymphoid cells of the normal condition. Individually they cannot be distinguished from the small round cells that appear in such great numbers in the stroma as the result of infection, as they can in mass. H. S. Gardner (Jour. Amer. Med. Assoc., Jan. 21, 1911).

When the congestion results suddenly from causes acting during or just before the menstrual period, it is also intense and accompanied by interglandular extravasation and blood-stasis that interfere with the menstrual discharge, and which, if not relieved, run into the chronic form.

In *acute septic* endometritis the blood-vessels of the endometrium are engorged and increased in number. There is considerable exfoliation and proliferation of the epithelial cells, sometimes to such an extent as to cause a superficial necrosis. The interglandular spaces are crowded with round cells, leucocytes, and cocci, which may extend into the muscularis mucosæ, and, if streptococci be present, a short distance into the uterine walls. Congestion, extravasation of blood, serous and round-celled infiltration take place throughout the uterine tissue, and a fibrinous exudate may appear on the peritoneal surface.

There is a more or less abundant flow of pus from the endometrium.

In *chronic septic* endometritis round cells and leucocytes crowd the interglandular spaces, compressing the glands, and in places penetrating and destroying them. After a time the formation of contracting adult connective tissue compresses and obliterates some glands, and obstructs the mouths of others, converting them into small cysts. The epithelium in the atrophic glands and on the surface also degenerates, so that in old and senile cases the mucous membrane may be represented by a thin layer of sclerotic connective with only vestiges of epithelial structure.

The uterine walls, at first hyperemic and infiltrated to a greater or less depth with serum and round cells, are thicker and softer than normal, but later, owing to the contraction of the inflammatory tissue, become hardened. The atrophy of the muscular tissue and absorption of the serum, as well as the senile changes, may finally lead to a diminution in size of the entire organ.

Endometritis occurring in connection with abortion may interfere with the atrophy of the decidua, and masses of decidual cells may be found in the endometrium in connection with the round-cell infiltration.

In some cases the menstrual congestion is so great that an acute attack is practically lighted up at each period. The stroma-cells are enlarged and resemble decidual cells, and the tissues are crowded with leucocytes. The congestion is so great that there is an abundant extravasation of blood in the interglandular spaces, which loosens the superficial portion to the extent of causing its exfoliation in places or even entire, as a more or less complete cast of the uterine cavity.

After the menopause the cervix may become stenotic, and the discharges be retained. The uterine cavity may then become distended, and the uterine walls attenuated by an offensive and purulent fluid.

PROGNOSIS.—The prognosis of acute interstitial metritis in the puerperal state or after abortion is grave. The patient may die of septicemia, or the disease may extend to the Fallopian tubes, ovaries, and peritoneum, or into the veins or lymphatics of the broad ligament, or it may result in chronic endometritis and subinvolution.

When not connected with pregnancy the disease seldom terminates fatally, but is apt to extend to the adnexa or become chronic.

Acute cervical metritis may end in recovery, but, as a rule, becomes chronic.

Chronic cervical metritis may get well, but, as a rule, it persists for a long time. It can ordinarily be cured either by local treatment or operation.

Chronic corporeal endometritis of the septic variety is apt to get well if there is good drainage through the cervix. Without adequate drainage it becomes chronic and is liable to spread to the adnexa.

In cases of long standing the septic condition can be removed, but the endometrium and myometrium can seldom be restored to a normal state.

The sterility is apt to be permanent.

Chronic glandular endometritis can generally be cured by treatment. Mild or recent cases may get well spontaneously, but severe cases usually persist for a long time, or until the menopause.

TREATMENT.—For *acute glandular metritis* due to suppression of the menses, the flow should be re-established, if possible, in the early or congestive stage. As soon as possible after the suppression the patient should take a **warm sitz-bath** (100° F.—37.8° C.), and go to bed. **Hot drinks, hot poultices to the abdomen and groins,** and **hot-water bags** or bottles **to the feet and legs** should be employed. In married women **scarification** of the **cervix** may be used with benefit. The production of slight nausea by means of **tartar emetic, ipecac,** or **lobelia** is useful as a sedative to the congested pelvic organs. If the menstrual flow is re-established by these means within a day or two, the patient may leave the bed after the flow has ceased, but should lie down two or three hours in the middle of each day, and take but little exercise for three or four weeks. At the time of the next period she should keep to the bed and repeat the hot applications, etc., if the flow does not appear on time. The bowels should be kept open by **salines.**

If the menses are not re-established within two or three days after their suppression, the patient should remain in bed for a week or ten days, apply **counterirritants** over the iliac and suprapubic regions, and take copious **hot douches** (115° to 120° F.—46.1° to 48.9° C.) two or three times daily in the recumbent posture. She should secure a daily evacuation of the bowels, and, if practicable, introduce small cotton **tampons,** saturated with a 10 per cent. solution of **ichthyol** in boiled glycerin, high up in the vagina every other day, and leave them for about eighteen hours. **Tonics** and an easily digested **diet** should be prescribed.

Acute septic metritis following labor or abortion calls for a thorough **evacuation of the uterus** by the *fingers* or dull **curette,** and, if septic symptoms persist, antiseptic **intra-uterine douches** every twelve hours (1:3000 of **corrosive mercuric chloride** followed by sterilized water or 1 per cent. **creolin**) and **vaginal douches** of the same character every six or eight hours.

When the attack follows an operation, an **ice-bag** should be kept on the lower abdomen for twenty-four or thirty-six hours, the infected surfaces be thoroughly disinfected by a strong antiseptic, and one of the above-mentioned antiseptic **douches** be used either to the endometrium or vagina as required.

As the inflammation subsides, **hot douches, laxatives, tonics, rest in bed,** etc., are indicated.

In chronic uterine inflammation all causes of the disease and all conditions that perpetuate it should receive attention.

> In puerperal septic endometritis the insertion into the uterine cavity of **tampons** of **iodoform** gauze soaked in 1 to 8 glycerin **ichthyol** and thickly powdered with **naphthalin** gives prompt and satisfactory results. Poliansky (Prakt. Vratch, May 31, 1903).

Displacements should as far as possible be corrected, stenosis relieved, and pelvic inflammatory conditions and tumors be treated or removed.

The patient should remain in bed during a portion or all of the menstrual period, and take more than ordinary care of herself after abortions or confinements.

Chronic glandular endometritis, alone or in connection with chronic septic or interstitial endometritis, and all menorrhagic cases uncomplicated by pelvic peritonitis should be curetted.

> Writer's method of treatment of chronic endometritis consists of free **drainage** of the organ and of its mucous glands with irrigations with various solutions. Preliminary **dilatation** is produced by the use of a mild **galvanic current** applied with an intra-uterine electrode, and followed by **irrigation** with galvanization. The current must be even and uninterrupted, the negative electrode being applied in the uterus. The galvanic current procures direct stimulation of muscular, glandular and secretory structures. Simple catarrhal endometritis produces a watery discharge, while the involvement of the cervix renders it thick and ropy. Proper treatment involves cleansing, opening the mouths of the glands, stimulating glandular activity, and replacing the normal equipoise between vascular supply, innervation and muscular relationship. All these are accomplished by galvanic irrigation. J. H. Rector (Med. Rec.; Monthly Cyclo. and Med. Bull., March, 1909).

When the **curette** is employed due care should be exercised. Rough manipulation and undue pressure upon the uterine surfaces have been followed by untoward results. Curettage should be avoided when there is tenderness in the tissues beside the uterus.

Exfoliative endometritis and polypoid endometritis may require more than one **curettage.**

In a large proportion of cases the cervical canal is small or bent, and must be kept **dilated** for several weeks subsequently to promote uterine drainage.

In others it is necessary to use strong **astringents** and **antiseptics** to the endometrium, for the purpose of counteracting the tendency to a recurrence of the hyperplasia or the sepsis.

The **hot vaginal douche** twice daily acts beneficially as a sedative to the pelvic circulation, and aids in keeping the vagina clean.

Local treatment may be commenced in two or three weeks after the operation. If the cervix is small or bent, a round **dilator,** or male **urethral sound** No. 12 to No. 15, should be passed through the internal os once or twice a week. In order to avoid infection, the patient should take a large, **hot vaginal douche** shortly before treatment, and the gynecologist should wipe out and disinfect the vaginal fornices and cervix through the speculum before introducing the disinfected sound.

After the sound is withdrawn a 50 per cent. solution of **ichthyol** in glycerin may be applied to the endometrium, or, if the case has been a hemorrhagic one, pure **lysol** or **carbolic acid,** or a 20 per cent. solution of **chloride of zinc,** every ten days to two weeks.

> Siredey's method, viz., the injection of a 12 to 1000 solution of **picric acid** into the uterine cavity by means of Braun's syringe used in 21 cases. The solution is prepared with hot water, allowed to cool, and decanted. It may be kept sterile for an indefinite time. The cervical canal is disinfected with cotton impregnated with iodoform-ether, and the syringe is introduced into the cervix, and about 2 c.c. injected into the uterine cavity. The vagina is **tamponed** with **iodoform gauze,** the plug being worn till the next day. The vagina is washed daily with a hot solution of **potassium permanganate.** The writer also disinfected the external genitals and irrigated the vagina before the introduction of the speculum. The cases were thus

treated until the gonococci disappeared. Picric acid proved very efficient and non-toxic and showed a marked anti-bacterial action against gonococci. The injections far from being caustic, were analgesic. Serra (Riforma Medica, June 24, 1903).

Good results obtained with **magnesium sulphate.** An ounce of the remedy in crystals is poured into the vagina and confined there until, by osmosis, it causes a free discharge from the pelvic tissues. This, if repeated daily for one week, will reduce a large, spongy uterus to normal dimensions. C. J. Wallace (Wisconsin Med. Jour.; Monthly Cyclo. and Med. Bull., June, 1908).

When there is a tenderness or irritation in the tissues beside the uterus, curettage and intra-uterine medication are liable to do more harm than good.

The American clinician has been too undiscriminating. For several decades he has been content to accept reports which neither conform to the clinical findings nor assist him in combating the disease (*vide* the diagnosis of "endometritis" constantly received for curettings from normal cases of anteflexion and stenosis merely sent to the pathologist as a matter of routine). It will suffice if we recognize in our reports: 1. A *premenstrual* or *secretory* stage. 2. A stage of *menstruation* (it will be found that mucosæ from cases of menorrhagia and metrorrhagia alike conform to this type). 3. An *interval* or *stage of comparative rest.*

Curettings of these types should be reported as "normal endometrium" with mention of the appropriate stage, regardless of whether the stage conforms accurately with the date of menstruation. 1. If, in addition, plasma cells are found, it is sufficient to report "endometrium showing chronic inflammation" and "cyclical stage 1," "2," or "3" as the case may be. 2. Borderline cases between physiological and pathological growth can be classified as "endometrium with exaggerated phase" in order to emphasize the fact that the change is purely secondary (ovarian influence). 3. Marked glandular cystic hyperplasia, hyperplasia after the menopause, etc., can be reported as such, without the use of the word "endometritis."

The clinician, on the other hand, should recognize 1. That *anatomical* evidence of inflammation is demonstrable in less than half of all cases. 2. That many cases which anatomically show the presence of inflammation give no corresponding *clinical* symptoms. 3. That a majority of cases which show the conventional symptoms of endometritis (leucorrhea or bleeding) are wanting in demonstrable anatomical signs of inflammation. 4. That, therefore, in most cases, we are obliged to search for other etiological factors to account for the symptom-complex hitherto called "chronic endometritis," and devise for it a more logical treatment than curettage, intra-uterine applications, or vaginal douches. R. T. Frank (N. Y. Med. Jour., March 30, 1912).

In such cases a copious **hot vaginal** douche (120° F.—48.9° C.) should be taken at or near the noon hour, followed immediately by two hours of rest in the recumbent position and another douche at bedtime, followed by the introduction into the vaginal vault of a **tampon** saturated with a 10 per cent. solution of **ichthyol** in glycerin. The tampon is removed when the noonday douche is taken.

Laxatives, tonics, massage, regulated **out-of-door exercise,** and **restriction of coitus** are useful adjuvants.

Endometritis with stenosis and pyometra (so-called senile endometritis) should be treated on the same principles as any pus cavity, viz.: **dilatation** of the **cervix** for drainage, and the washing out of the uterus with **antiseptic solutions** once or twice daily.

In *lacerated cervix,* the presence of endometritis, with marked eversion and hypertrophy of the mucous membrane, indicates the use of special measures before trachelorrhaphy is undertaken.

The patient's **diet** should be regulated, constipation corrected, and measures instituted to relieve the accompanying anemia. She should take twice daily a **vaginal douche** of hot water containing an ounce (30 Gm.) of rock salt to the quart (liter). The cervix should be scarified or punctured and all obstructed Nabothian glands entered and their cavity painted with Churchill's tincture of **iodine**, a combination of iodine tincture **and creosote** (two to one), iodine crystals dissolved in 95 per cent. **phenol**, **silver nitrate** or **zinc chloride** (1 dram —4 Gm.—to the ounce—30 c.c.), or a solution of **argyrol** or **pyroligneous acid.** The superfluous material should be sponged away and a **tampon** applied beneath the uterus, consisting of plain sterilized gauze and cotton, or **gauze** medicated with **iodoform, phenol, boric acid,** or **thymol.** The tampon may be medicated with preparations of **glycerin,** a 50 per cent. solution of **boroglyceride,** the official **iodoform** ointment, a 10 per cent. solution of **ichthyol,** or 25 per cent. of ichthyol in hydrated wool fat.

The local treatment, with the tampon, should be employed twice a week, and the tampon removed at the end of forty-eight hours, to be followed twice daily by a **vaginal douche** of ½ gallon of hot **salt water** (110° to 120° F.—43.3° to 48.9° C.). Where the cervix and neighboring tissues contain much inflammatory exudate the bulb (Davidson) syringe, by the force of its current, exercises a salutary influence in promoting absorption. Intracervical or intra-uterine applications should not be made unless the cervical canal is quite patulous, so that the fluid or increased serous discharge can escape readily. If the canal is obstructed by hypertrophied and everted mucous membrane, **gauze packing** or the use of a **laminaria tent** will render the application more effectual and safe.

Irregular bleeding or *profuse leucorrhea* indicates the use of the sharp **curette** and **dilatation.** The uterus should be irrigated during or after curettement with a solution of **bichloride,** 1:3000; **formalin,** 1:1000; a **hot salt solution,** 4 drams (16 Gm.) to 2 pints (1 liter), or, preferably, with 1 per cent. **salt solution,** and swabbed with a saturated solution of **iodoform** in ether. If much bleeding follows the curettement the uterine canal should be packed with **iodoform gauze.** Montgomery (Pract. Gynec.; N. Y. Med. Jour., Feb. 17, 1912).

Chronic cervical endometritis should be treated by local applications made through the vaginal speculum. Simple and papillary erosions yield quickest to astringent and stimulating remedies, such as **phenol, creosote,** and strong solutions of **chloride** or **persulphate of iron.** Follicular cervicitis yields quickest to iodine applications. A mixture of 2 parts each of **iodine** crystals 95 per cent. **phenol,** and 1 part of **glycerin** is efficacious, and should be applied twice weekly. Retention cysts should be punctured before the application is made. Antiseptic and astringent douches, such as a 1:2000 solution of **permanganate of potassium** or of **chloride of zinc,** may be employed with benefit twice daily.

In *gonorrheal cervicitis* and *endometritis* the following treatment is indicated. *Acute cases:* 1. Confinement to bed. 2. Keep emunctories active. 3. Limit **diet.** 4. Cleanse vagina frequently with large amounts of hot **saline solution** or **hot water** containing **boric acid** or a weak **iodine** solution. Use irrigator with nozzle projecting a straight forcible stream, and pinch mucous membrane of introitus around nozzle, to flush cavity satisfactorily. Intra-uterine measures and pelvic operation intervention contraindicated. *Subacute cases:* 1. Soften and dilate cervix with Goelet's uterine **electrodes** and **galvanic** current. 2. Flush uterine cavity with hot **iodine solution,** 1 dram (4 c.c.) of the tincture to a quart of water, or **silver nitrate,** 1:5000. 3. As condition improves, substitute daily intra-uterine injections of iodized **phenol** (equal parts of iodine tincture and phenol) or 1 per cent. **silver nitrate.** Use syringe with long pliable nozzle, with its tip wrapped with cotton; inject fluid into cotton and withdraw syringe. Insert **iodine-glycerin tampon** (1 dram to 4 ounces), which patient is to remove next morning. Remove cotton within uterus at next visit. *Chronic cases:* 1. **Puncture, evacuate,** and **sterilize** diseased Nabothian glands. 2. Touch opened glands and erosions about os with pure **iodine** tincture. 3. **Intra-uterine irrigations** and **injections** as above, three times weekly. 4. **Curettage** of uterus, thoroughly scraping internal os and cervical canal, followed by swabbing with **iodine tincture** and appropriate after-treatment. Dannreuther (Med. Record, Nov. 4, 1912).

Henry T. Byford,
Chicago.

ENDOTHELIOMA. See Cancer.

ENTERIC FEVER. See Typhoid Fever.

ENTERITIS. See Intestines, Diseases of.

ENTEROCLYSIS. See Sodium: Saline Solution.

ENTEROPTOSIS. See Intestines, Diseases of.

ENURESIS.—DEFINITION.—An involuntary discharge of urine or incontinence of urine which may be due to many different conditions.

SYMPTOMS.—If we may speak of the symptomatology of this affection, which in itself, in the majority of instances, is to be regarded as a symptom, rather than as the actual disease, the ground is amply covered by the single statement which is usually detailed by the parent or the patient, that there is an involuntary passage of urine.

It is not very difficult to discover the presence of enuresis, but the determination of the cause or the causes for its existence is by no means so easy and is sometimes rendered impossible. Enuresis is not liable to be mistaken for any other affection, with the single exception of the incontinence, or overflow, symptomatic of retention of urine due to prostatic enlargement or some other obstruction to the genitourinary track, from the bladder, outward.

ETIOLOGY.—Incomplete development of the sphincter muscles, existing in the infantile period, may persist for an abnormal time (beyond the second year); when this occurs, it is followed by the involuntary emission of urine. This may be due to insufficiency of the sphincter vesicæ muscle, which allows the urine to enter into the upper part of the urethra; it is expelled by a reflex action of the detrusor urinæ muscle.

Enuresis may also be caused by debility of the neck of the bladder and of the internal sphincter, or through its inadequate control from disease of the spinal cord and of the nerve-centers; and also through overdistention of the bladder with urine.

In a number of cases enuresis may be a local manifestation of a general lack of tone of the entire muscular system. Many cases suffer from marked nutritive disturbances attributed to reflex causes alone. Even where there are no gross evidences of malnutrition, the metabolic activity in the sensitive nerve-cell is probably disturbed (McKee).

Enuresis may be the result of fatigue, *i.e.,* of sleep so profound by exhausted children that the desire to urinate did not, as in cases witnessed by the writer, awake them as under ordinary conditions. A little care on the part of the parents prevented this

> overfatigue and speedily cured the enuresis. Nicoletopoulos (Arch. de méd. des enfants, Sept., 1910).

In cases of hypothyroidia the impaired oxidation due to inadequate activity of the thyroid entails impairment of muscular power, including that of the sphincter muscles as emphasized by Hertoghe, Sajous and others.

> In many cases there is deficiency of the thyroid gland secretion. If carefully looked for many of the stigmata of cretinoid degeneration will be found in these patients. Particular stress is laid by the writer on the following in this connection: (1) a persistently subnormal temperature; (2) a deficiency in height and weight; (3) abnormalities of the skin and its appendages, more especially the hair, not only of the head, but also and particularly of the superciliary region. Leonard Williams (Adenoids, Nocturnal Enuresis, and the Thyroid Gland, 1909).

Diseases of the nervous system, both functional and organic, are recognized as factors in producing this disease. According to Rachford incontinence of urine in children is a true neurosis and not, as a rule, due to muscular incompetency of the sphincter vesicæ. It rests upon excitability of the nerve-centers produced by heredity and age; anemia with consequent malnutrition, increasing the excitability of the nerve-centers, and reflex irritation. Anesthesia of the bladder has been noted in a large proportion of cases by Ozerezkowski.

> The more we analyze enuresis, the more the clinical picture gives the impression of being essentially a developed habit, and a concomitant stuttering or *tic convulsif* sustains this impression. Enuresis includes many features which unite it with the tics or habit spasms. First, habituation; second, it is almost continuous; the bladder tends to empty itself whenever a small quantity of urine has accumulated. The predominance of nocturnal incontinence is due to the absence of distracting influences during sleep, for it is well known that a habit spasm is temporarily suspended when the patient's attention is directed thereto. During the day, the victim of enuresis is powerfully restrained by the force of public opinion and ridicule, though he may forget himself and lose control under some special strain or excitement. Third, there is the frequent association of enuresis with such unquestionable habit spasms as stuttering. Fourth, the age of onset agrees precisely with that of the other habit spasms; the ages of maximum frequency also correspond. Its lesser tendency to persist into adult life is due to its involving the genitourinary tract, which undergoes such radical anatomical and physiological changes at puberty. Furthermore, some cases of enuresis, especially in females, do persist into adult life, and then become exceedingly difficult to cure, as also happens with other tics. Wachenstein (N. Y. Med. Jour., Feb. 5, 1910).

Heredity is a potent predisposing factor in many cases. Monro reported as an example, a family in which the 6 children inherited the disorder from their father. The 2 elder children, girls, are always more affected toward the menstrual period. The incontinence affected most all of the children alike by day and night. Two of the children were subject to fits, which began during early childhood; and they showed also other signs of degeneracy. Enuresis is frequently associated with epilepsy and with affections of the spinal cord.

> Enuresis is often due to some general nerve condition, for most children suffering from it are children of neurotic parents. Other nervous dis-

orders are frequently present. Epidemics are very frequent in institutions in which many children are brought into close contact. Thiemich (Berl. klin. Woch., July 30, 1901).

In certain obscure cases enuresis is the result of an occult spina bifida, which in turn is due to defective development of the spinal cord. Examination of 22 adults with enuresis and 20 children by the Roentgen rays confirmed this assumption of defective development of the spinal cord and spine as an important factor in the enuresis. It was pronounced in 68.2 per cent. of the adults and in 35 per cent. of the children. Fuchs (Deut. med. Woch., July 6, 1911).

As to the local conditions which produce incontinence, there may be mentioned, overdistention of the bladder with urine; hyperacidity of the urine; cystitis; phimosis, or an adherent prepuce, either of the glans penis or of the clitoris; nephritis; pyelitis; vesical and renal calculus; glycosuria, and rectal irritation.

The writer observed 2 cases of nocturnal incontinence occurring as an early symptom of renal tuberculosis. In 2 other cases nocturnal incontinence appeared after nephrectomy. Constantiesco (Jour. d'Urologie, May, 1912).

Contraction of the bladder may cause incontinence. Robson reported the case of a single woman, aged 30, in whom bimanual examination revealed that there was practically no bladder, it being merely represented by a small, hard lump about the size of a walnut.

Masturbation has been regarded as a prolific cause of enuresis; but the frequency of this habit in children would tend to suggest that the two disorders may occur coincidently rather than that there exists a causal relationship between them. In girls friction of the clitoris is a local irritation which, acting reflexly as does phimosis on this organ, might cause enuresis.

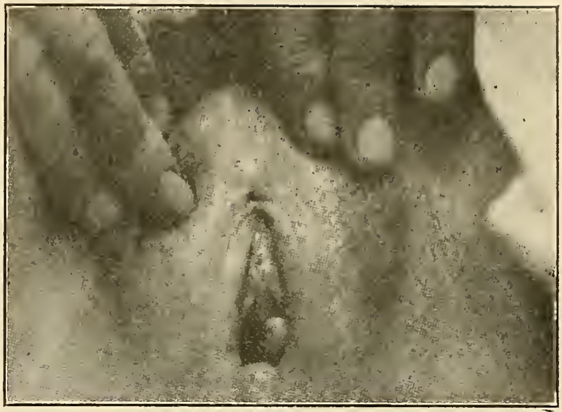
Three years' observation in the State Industrial School showed that in institutions, at least, enuresis is directly due to masturbation in about 90 per cent. of all cases. Seventy-five cases of enuresis were observed in a total school population of from 800 to 900 pupils between the ages of 10 and 21 years. Beilby (Amer. Med., March 5, 1904).

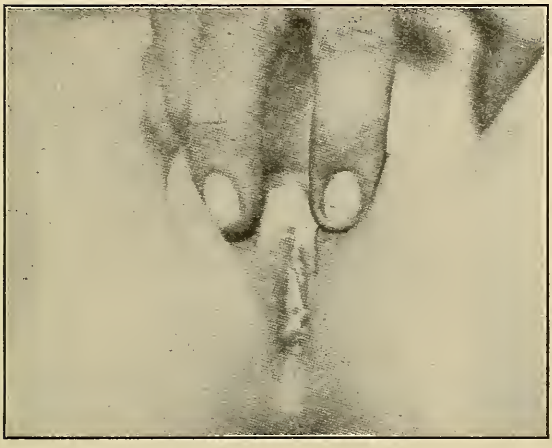
An examination of the clitoris should always be made in all gynecological cases as well as in children who habitually handle the parts. Series of cases of enuresis in both children and adults successfully treated by **circumcision.** In the 9 cases cited, the following points were of interest. Of the 4 mothers on whom circumcision was performed, 3 had borne children who had inherited a similar anomaly; 1 mother, whose children were normal. There were 3 children in whom the mother's condition was unknown, and 2 children whose mothers suffered from a like condition. In every instance the condition for which the operation was done was not only relieved, but permanently cured. Three of the cases are shown in the annexed cuts. C. E. McGirk (Surg., Gynec., and Obstet., Nov., 1907).

Children are liable to fissure of the anus with far greater frequency than is generally believed, and this may excite involuntary urination. Constipation and the presence of worms (mostly ascarides) are among the more common causes of this disease.

With regard to causation, enuresis may be roughly divided into 5 groups: (1) genitourinary, (2) nervous, (3) malformations, (4) general, and (5) idiopathic. As regards the first the urine may be at fault; there may be hyperacidity or excessive alkalinity, or there may be bacteriuria. Inflammation of various parts of the genito-

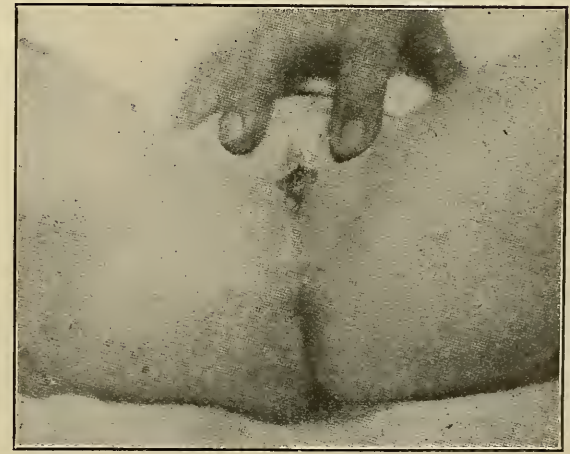
Mrs. S., aged 22 years.





Gladys D., aged 4 years.

Elizabeth W. aged 5 years



Phimosis as a cause of enuresis in the female. (*McGirk.*)

> urinary tract, calculi, new growths, etc., may be responsible for the disorder. The nervous causes are very numerous and many are reflex in character, such as balanitis, vulvovaginitis, worms, etc. Malformations of the spinal cord or of the genito-urinary organs may be accompanied by urinary incontinence, and treatment in such cases is particularly hopeless. As general causes may be mentioned rheumatism, thyroid insufficiency, diabetes, etc. Still found enuresis associated with rheumatism in about 5 per cent. of his cases. J. Allan (Prescriber, Aug., 1912).

Enuresis may follow labor owing mainly to the traumatism, pressure, etc., to which the bladder, the glands, and the urethra are subjected during the process.

PROGNOSIS.—When the cause can be discovered and removed, the prognosis is favorable; in elderly people, however, the affection is generally due to paralysis or deep-seated disease of the urinary organs. The outlook is usually favorable in cases of enuresis nocturna. Sometimes, however, it proves to be a very obstinate malady.

TREATMENT.—The cause of the disorder should be discovered and its removal effected.

Atonic conditions, in children as well as in adults, often lie at the foundation of the lack of control over the passage of urine, and, in these cases, **outdoor exercise** should be advised and a carefully selected **diet** prescribed for its nutritiousness and digestibility. A vegetable diet has been advocated.

> Children fed on an excess of starchy foods as a rule pass a larger quantity of urine than do those who are not so fed. When all other measures fail, it is well to put the child on a rigid **antidiabetic diet** for a few days and to watch the result, which is often gratifying. Starchy food may be allowed for breakfast, but not afterward. Even small quantities of bread and cake at supper may renew the enuresis after it has been checked. **Tonic treatment** should also be used. Lewis (Brit. Med. Jour.; Med. Rev. of Rev., Sept., 1912).
>
> Vegetables contain a large proportion of water, which tends to reduce thirst, while the stools on a vegetable diet are abundant and very soft, so that a large proportion of the fluid output occurs by way of the intestines instead of the kidneys. A **vegetable diet** is thus the ideal diet for children with enuresis nocturna. Coffee, beer and all alcoholic drinks are contraindicated and milk should be restricted; fully 600 of 1000 parts of milk pass out of the system in the form of urine. If there is much thirst, fruit should be given rather than fluids. A very important measure in treatment of enuresis, second only to restricting the intake of fluids after 4 P.M., is to **raise the foot of the bed** and make the child sleep on its side, possibly by tying a brush to its back which hurts if he rolls over on it, and systematic **waking up** of the child to have it **urinate regularly.** Most of the children addicted to enuresis are exceptionally hard sleepers and they are not aroused by the desire to urinate. This can be remedied by having the child take a **nap** for two hours, **morning and afternoon.** Klotz (Deut. med. Woch., Dec. 5, 1912).

Medicinally, the use of ferruginous preparations are indicated where any degree of anemia exists. The syrup of the **iodide of iron** is readily taken by children. For adults, the **pepto-mangan** (Gude) is an excellent tonic. The dose of the first is from 3 drops upward, well diluted with water; and of the second a dessertspoonful to a tablespoonful, in milk or wine. Jacobi speaks highly of the **elixir pepsinæ,**

bismuthi, et strychninæ of the National Formulary, in insufficient gastric digestion associated with atony of the stomach; a child of 3 years taking a teaspoonful three times a day.

> In enuresis of digestive origin, the condition is intermittent and irregular, alternating with normal periods. There is unusually sound sleep, and, generally, some mild inherited nervous taint. The children are unusually large eaters; the mother prides herself on the child's fine appetite, but there are always slight digestive disturbances. Treatment is of the simplest, merely **reduction of the amount of food,** and not letting the children have any liquid or any foods that ferment readily. **Mild laxatives** are useful and also, possibly, light **massage** of the **abdomen** and **hot-water compresses.** A. Collin (Jour. d'Urol., Jan., 1913).

Incontinence due to a weakness of the sphincter muscle is best relieved by ascending doses of **strychnine** or the tincture of **nux vomica.** In appropriate cases, strychnine is a very efficient agent.

Douching of the **perineum with cold water** is advised by some writers as a very efficacious measure. It is not a disagreeable procedure if care is taken to concentrate the douche on the genitoanal region.

> In both diurnal and nocturnal enuresis in children the sudden **cold douche** to the anal and **perineal region** is very effective. It may be done on a special chair with open seat. Klotz (Berl. klin, Woch., May 1, 1911).

The application of the **faradic current,** one electrode being placed in the rectum and the other over the perineum in the male and the mons veneris in the opposite sex. The current is to be gradually increased. Or, as advised by Cipriati, a sound, the end of which formed an electrode, is introduced into the urethra as far as the sphincter of the bladder, and its free end is attached by a chain to one of the Leyden jars; the machine is regulated to give 6 to 8 sparks a second, and each sitting lasts five minutes.

If incontinence is due to hyperesthesia of the mucous membrane or irritability of the bladder, the remedy indicated is **belladonna.** Baruch, Watson, and other observers bear testimony to the efficiency of this drug in the treatment of the nocturnal form of incontinence. Both belladonna and atropine are tolerated in much larger doses by children, in proportion to their size or age, than by adults. In many cases a single evening dose of the extract of **belladonna** (gr. ¼ to ¾ to 1—0.016 to 0.048 to 0.065 Gm.) or of the **sulphate of atropine** (gr. $\frac{1}{100}$ to $\frac{1}{75}$—0.0006 to 0.0008 Gm.) answers sometimes to an unexpected degree, according to Jacobi. In most cases, however, belladonna or its alkaloid must be pushed to the extreme limit before an impression is made upon the disease.

> **Belladonna** should be given in the form of a suppository, as it interferes much less with the appetite and digestive system. Fleischner (Calif. State Med. Jour., Feb., 1911).
>
> Two varieties of the complaint have to be recognized: (*a*) the atonic variety. and (*b*) that characterized by vesical irritability. In the latter antispasmodics are especially useful, and among these **belladonna** comes first. The general consensus is that this drug must be given in large doses and pushed until signs of intolerance, such as dryness of the mouth, mydriasis, disturbances of vision, etc., are just in evidence. For a child

over 5 years of age 10 minims (0.6 c.c.) tincture of belladonna may be given thrice daily; this dose is increased by 2½ minims (0.15 c.c.) every few days until the full physiological effects of the drug are apparent. J. Allan (Prescriber, Aug., 1912).

In cases in which the urine is normal the treatment consists in improving the general condition of the child. Then **belladonna** should be given, beginning with 10 minims (0.6 c.c.) of the tincture two or three times a day, gradually increasing the doses up to 20 to 25 minims. The writer has never given larger doses, but he has used approximately larger doses of **atropine.** Even with the smaller doses of belladonna the child may complain of difficulty in seeing, dry mouth, etc., and when such is the case one must proceed carefully before increasing the dose. The writer, however, has never had very much trouble with belladonna, but once or twice with atropine he has witnessed well-marked symptoms of poisoning. With the great majority of patients he does not prescribe beyond 15 minims (0.9 c.c.) of the tincture of belladonna thrice daily, but it is advisable to continue this for a considerable period.

When the urine is extremely acid, loaded with urates, etc., one must first reduce the acidity of the urine. This is most easily accomplished by the use of **citrate of potash** in doses of 10 grains (0.6 Gm.) thrice daily; though larger doses may be required. When the acidity has been reduced, the belladonna should be begun. If the child's general health is not very good, 2 or 3 minims (0.12 to 0.18 c.c.) of liquor **strychnine** added to the prescription is often beneficial. It is inadvisable to give meat when the child is suffering from this "acid" condition. When the urine is alkaline, contains pus, albumin, etc., **dieting** is of the first importance, all carbohydrate food as far as possible being prohibited. If the urine is very alkaline, **acid sodium phosphate** may be given; when the alkalinity of the urine has been reduced **belladonna** should be used in the manner stated above.

When bacilli occur in the urine a pure culture of *B. coli* is frequently obtained. If the urine is very acid it is wise to reduce the acidity by giving **citrate of potash,** then **urotropin** in 5- to 10- grain (0.3 to 0.6 Gm.) doses thrice daily often proves of immediate benefit. If there is mixed infection **salol** is often more efficacious. Mixed infection cases are often very troublesome, however, and a **vaccine** may sometimes be used with great advantage. Simpson (Edinburgh Med. Jour., Jan., 1913).

Habit, which Tyson mentions as sometimes the cause of enuresis in children, may be corrected, as suggested by this author, by encouraging the cautious practice of holding the water.

The method of **conscious repetition of Brissaud** was found useful by the writer. He had the patient urinate at regular stated times, but every time he does so he is directed to void a little, say 2 drams, and then stop; then void 2 drams more and stop, and so on, until the bladder is emptied. In this way the individual exercises the mechanism which controls urination; he trains and educates himself in the voluntary execution of the act. After this has been done two or three times under the direction of the physician the patient can carry out the exercise which should be persisted in. Herman (Archives of Pediatrics, Aug., 1910).

Masturbation, phimosis, adherent prepuce, rectal affections, etc., must receive appropriate treatment, after which the incontinence of urine, if it persists, will demand attention. In some cases, the bladder is abnormally small and requires **mechanical dilatation.** Haven reported 2 cases in girls cured by gradual **distention of the bladder** with a 4 per cent. **boric acid**

solution. Both were 18 years old, and from earliest infancy had wet the bed nightly, and found it impossible to retain the urine for more than a few minutes while awake. The bladder of both was abnormally small; that of the one held 8 ounces under pressure, that of the other only 3½ ounces. The treatment consisted in distending the viscus until discomfort was produced, after which the patient held the fluid as long as possible: ten to fifteen minutes in the beginning, though this time was doubled later. Distention was practised every other day, and improvement was rapid. Treatment was continued until the bladder would hold 20 ounces, and then, all symptoms having been relieved, it was discontinued.

Sir Henry Thompson strongly advocates the application of **nitrate of silver** to the urethra, whether in the male or the female. He states that the use of a **flexible bougie**, small, of course, for children, passed daily, and removed in a minute or so, is sometimes successful.

If this fails, the injection by means of a sufficiently long tube of the **nitrate-of-silver** solution to the prostatic portion of the urethra and neck of the bladder is a remedy of no mean value. For young women up to the age of 18 or 20 in whom this malady still exists, Thompson has found this treatment almost invariably successful. It should be applied immediately after the bladder is emptied, in quantity, say, of a dram (4 Gm.), and of a minimum strength of 10 grains (0.6 Gm.) to the ounce (30 c.c.), up to treble that strength if necessary for subsequent application. Enough should be employed to produce smarting, which should continue for a day or so. A week or two should elapse between each application.

Some authors advise **blistering the perineum**, others the use of the **actual cautery**, touching the same at several points around the anus. J. William White and Edward Martin state that when a habit of nocturnal incontinence is due originally to carelessness —the child, though awakened by the desire to urinate, prefers to wet the bed to getting up—that such cases may be cured by having the patient waked at about 1 or 2 in the morning, or at an hour before the habitual time of involuntary micturition, and made to empty the bladder.

> It should be treated as *tic convulsif.* The most successful treatment of tic consists in making the patient perform voluntarily under his own or some other person's control, the movement which has been so frequently repeated subconsciously. The child is compelled to **urinate at regular hours** during the **day,** and wakened at regular intervals during the **night,** the intervals being timed so as to anticipate the involuntary act, if possible. Thus, in a moderately severe case, micturition might be enforced on arising, at nine, noon, three, six, at bedtime, an hour after bedtime, and two hours after bedtime; bad cases may require a two-hour interval during the day, and more rousings at night. The essential matter is the accurate observance of the exact hour day by day. Often the training cure, by itself, proves ineffective; a common complaint being that the child is found to be wet every time it is roused, the tic being fully developed and practically continuous during sleep. Here we may aid by **cutting off all fluids** during the **later afternoon and evening,** thus reducing the secretion of urine to a minimum by keeping the bladder as nearly empty as possible. The writer always anticipates by **including** the

> deprivation of fluids in the plan of treatment, and, in addition, restricts the bulk of the evening meal, even in cases that seem relatively mild.
>
> As to auxiliaries **atropine** has a certain adjuvant value, and may be given rather liberally, for small doses are useless. When the tic is, as often happens, associated with a general run-down condition **tonics** are indicated. **Removal of adenoid vegetation** or greatly **hypertrophied tonsils** if present, is indicated, but a conspicuous effect on the enuresis need not be expected, save that the operative shock or the anesthesia may check it, as it may any habit spasm. It is wise to continue the training for a considerable time, at least two months, after the incontinence has ceased. Wachenheim (N. Y. Med. Jour., Feb. 5, 1910).

Among other remedies employed in this affection are **antipyrine, rhus toxicodendron, potassium bromide, monobromide of camphor,** and **ergot.**

With **ergot** I have had personal and very favorable experience.

The fluid extract of **rhus aromatica** has been recommended by Carpenter, Freyberger, and others. Freyberger's method consists in regulating the **diet,** advising the patient to sleep on a **hard mattress,** the use of light coverings, and **cold sponging along the spine.** The parents are directed to take their children up once or twice during the night, and to make them pass water.

The dose employed was:—

Five to 10 minims (0.3 to 0.6 c.c.) for children 2 to 5 years old.

Ten to 15 minims (0.6 to 0.9 c.c.) for children 5 to 10 years old.

Fifteen to 20 minims (0.9 to 1.2 c.c.) for older children.

A very convenient formula being:—

℞ *Ext. rhus aromatici liq.*. ♏x (0.6 c.c.).
Syrup. aromatici ...... ♏xx (1.2 c.c.).
Aq. destillatæ, ...ad ʒj (4.0 c.c.).
Sig.: Three times a day.

Thirty-three days on an average were sufficient to produce a permanent cure; fifty-three days to effect a permanent improvement in about one-third of the cases treated.

Where abnormally frequent urinations are due to disturbances in the bladder innervation, Fernand Cathelin, of Paris, devised the operation of **epidural injections** of **saline solution** and obtained good results.

> Eight cases treated by the writers by Cathelin's method at the Manhattan Hospital West for the insane. All were adult women and had histories of wetting the bed and clothing frequently for some time previously. The injections are made into the sacral canal between the periosteum of the vertebræ and the dura mater. The canal is reached through its opening in the sacrum. The patient is placed in the Sims position, the area sterilized, and the small osseous tubercles just below and to either side of the last palpable sacral spinous process are made out. The needle of an aspiration syringe is then thrust through the skin, drawn tightly between these two tubercles, the needle being held at an angle of 40 degrees to the sacral curve until it passes through the membrane covering the opening of the canal, when it is lowered to 20 degrees and pushed on into the canal. Five centimeters (80 minims) of sterile salt solution were usually injected at first and later 10 or even 15. These injections were made at intervals of about one week and favorable results following immediately in all 8 cases upon whom the injections were made. These cases have not been followed very long, but most promising results have thus far been obtained. The injections seem to be in nowise dangerous to the patient, and are no more painful than any hypodermic injection. The immediate effects are rarely even disagreeable. Valentine and Townsend (Med. Record, Sept. 26, 1903).

The writer obtained several favorable results by means of retrorectal **injections** of normal **saline solution** in amount up to about 6 ounces (180 c.c.). The needle is inserted just anterior to the coccyx, a finger having been placed in the rectum in order to protect this viscus. To obtain the best results of the treatment several injections may be necessary. It is indicated in those forms of incontinence of which the causation is not obvious. Jaboulay (Tribune méd., vol. xli, p. 202, 1908).

Cathelin's method of injection of **salt solution** applied in 22 cases of involuntary micturition at night in children, and good results obtained in about half the cases. The writer is convinced, however, that the effect was due to suggestion, and that probably equally good results can be obtained by the usual measures supplemented by suggestion without the necessity for the epidural treatment. Allaria (Gaz. degli Ospedali, April 27, 1909).

Subcutaneous injections of **saline solution** into the anterior perineum, 60 to 70 Gm. (2 to 2⅓ ounces) being used at each sitting—enough to cause a swelling the size of an egg. The pain is very slight and the results are excellent, since adults who from infancy have been given to wetting the bed awake with the desire to urinate, and do so without trouble, and into an appropriate vessel. Cahier (Arch. de méd. et de pharm, militaires, June, 1909).

The epidural space is a favorable route for absorption of a drug on account of the abundance of veins in the region, permitting much more rapid and extensive absorption than by the subcutaneous or gastric route. Case in which injection of less than 5 c.c. (80 minims) of physiological **salt solution** at blood temperature cured completely life-long nocturnal incontinence in a girl of 14, otherwise healthy. There has been no recurrence. The writer followed Cathelin's directions in every point, and commends the epidural injection, after failure of all other measures. G. Sisto (Annales de méd. et de chir. enfants, March 1, 1910).

Organotherapy has given excellent results in well-selected cases, *i.e.*, those in which there is evidence of lymphatic temperament, hypothyroidia or deficient metabolic activity or oxidation as represented by weakness, pallor, puffiness, obesity or mental dullness—all of which symptoms may occur simultaneously.

In 134 cases of urinary incontinence treated with the substance of the **suprarenal gland,** 66 were cured, 21 were improved, 14 were better during the duration of the treatment, 21 were not changed; in 12 cases the statements were not sufficiently accurate for classification. The best results were obtained in those cases which came under treatment early, while a considerable share of the failures were due to deficiencies in the treatment, especially too short a duration.

The treatment should be interrupted for several days at a time, in order to guard against habituation, and the dosage of the remedy must not be too small. The only ill effects obtained by giving these preparations on an empty stomach were slight abdominal pain and a tendency to vomit. These symptoms promptly subsided when the dose was diminished. Zanoni (Med. Standard, Nov., 1908).

Nocturnal incontinence of urine in young children and adolescents is due to thyroid insufficiency. Several cases in which the use of **thyroid gland** was followed by improvement or cure. Children who suffer from incontinence are almost always undersized, and they present the infantile habitus in varying degrees—improperly placed teeth, nasopharyngeal adenoids, flat chests, and emaciated and slender extremities. Such patients are often flat-footed and their feet have an offensive odor, their gait is stiff, they suffer from pains in the thighs and from sciatica produced by the cold and moist surroundings in which they lie at night. The systematic examination of the urine in these cases shows an abundant deposition of the cells covering the free surface of the mucous membrane of the bladder. In children beyond 2 years of age the writer gives three 5-grain tablets of thyroid extract each week with from 3 to 5 grains (0.2 to 0.3 Gm.) of **potassium iodide** and **bromide** daily. Hertoghe (Bull de l'Acad. royale de méd. de Belgique, xxi, No. 4, 1907).

Series of 25 cases in which relief was afforded by means of small doses of **thyroid gland.** The suggestion was obtained from the case of a boy with nocturnal enuresis who instead of improving on removal of adenoids and tonsils became worse. The therapeutic effect of thyroid extract "was most drastic." The enuresis ceased immediately and never recurred. It is important that the dose of thyroid gland be small—from ½ grain to 2½ grains (0.03 to 0.16 Gm.) thrice daily—as larger doses may defeat the purpose of the treatment, as was illustrated in one case in which enuresis previously absent developed in a boy to whom 2½ grains (0.16 Gm.) of thyroid extract were administered thrice daily for the correction of general debility following an attack of nephritis. The initial dose should be small, and it should be increased only if necessary, but no more should be administered than the minimum sufficient to effect the desired result. Leonard Williams (Lancet, May 1, 1900).

Ten patients received the following treatment. One-fourth grain (0.016 Gm.) **thyroid gland** was given three times a day, increasing to ½ grain (0.03 Gm.) three times a day. Fluids were not allowed after 4 P.M., and the foot of the bed was decidedly elevated at night. Of these 10 patients, 8 improved; 2 did not improve. Of the 8 who improved, in 4 cases circumcision had been previously performed without result. Fleischner (Calif. State Jour. of Med., Feb., 1911).

Enuresis is sometimes associated with a special form of infantilism or hypoplasia due to thyroid insufficiency. **Thyroid gland** in small doses—½ to 2 grains (0.03 to 0.12 Gm.)—will usually relieve the enuresis. The dose should be decreased or omitted if rapid pulse, fever, or other toxic symptoms arise. In cases not responding well, alternate thyroid with calomel, 1/10 grain (0.006 Gm.) *t. i. d.* Relief is usually obtained in a month or two, but some cases require further medication to improve general condition. Also supervise child's **exercise, diet, bathing,** etc., and guard against physical or mental strain. McCready (Penna. Med. Jour., Jan., 1911).

Series of 28 unselected cases of enuresis were treated with **thyroid gland.** Of these 16 showed marked improvement or were cured, and 12 did not improve at all. As the children were only seen once weekly the drug was cautiously given, the initial daily dose being ¼ or ½ grain (0.016 or 0.032 Gm.). The cases which appear to react to this form of treatment better than all others are those in which the enuresis has persisted since birth, and in which the patients are also backward. A. C. D. Firth (Lancet, Dec. 9, 1911).

The connection between nocturnal enuresis and adenoids has not been generally recognized. Out of 716 cases of adenoids operated on by Fisher, 14.8 per cent. were troubled with enuresis. Mygind reported 7.75 per cent. out of 400 cases and Grüback 14.28 per cent. out of 427 cases. Hamonic circumcised in 187 cases of phimosis suffering from incontinence of urine with 130 cures. Of these, 47 were cured in twenty-five days, 83 within forty-two days and the remainder were lost sight of.

The writer has likewise obtained good results from **thyroid.** He also

> recommends 20 drops of fluidextract of **ergot**, *t. i. d.* for a child 5 years old; as a bladder tonic and for irritability at the neck of the bladder he gives $\frac{1}{400}$ to $\frac{1}{300}$ grain 0.00016 to 0.00021 Gm.) of **atropine** an hour or two before retiring. John Ruhräh (Amer. Jour. Med. Sci., Feb., 1912).

The application of **collodion** over the opening of the urethra has, in Somways's experience, been found effective in cases of nocturnal enuresis; the pressure of the urine awakens the child, and it thus becomes gradually weaned from the habit of bed-wetting.

The injection of **paraffin** parallel to and along the urethra, or around it, a method introduced by Gersuny in 1900, has been found of value in relaxation of urethra, loss of tone of the sphincter, laceration or lesions compromising its efficiency as a canal.

> Case of a woman who had been subject for six years to incontinence of urine, apparently of traumatic origin. It became so complete as to prevent her working for a living. There was a posterior colpocele without prolapse of the anterior vaginal wall; the uterus lay a little below the normal level. The urethra was intact, but its sphincter had lost its normal tone. In order to narrow the relaxed urethral canal and to afford a resisting medium upon which the sphincter might act, the author injected solid **paraffin** into the urethral canal after Gersuny's method. The incontinence disappeared in a few days, and did not return. Fabre and Trillat (Ann. de Gynéc. et d'Obstet., Sept., 1908).
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> The final outcome is known in 2 of the cases; in 1 of Gersuny's, after an interval of three years and in the writer's case, after nearly two. In the latter case a woman of 32, the **paraffin** was found apparently unmodified where injected, answering its purpose just as well after nearly two years as it did at first. He injected a total of 9 or 10 Gm. (2¼ to 2½ drams) of paraffin with a melting point at 42° C., at six sittings. The fluid paraffin was taken up into the syringe and was allowed to cool to the consistency of a thin salve to avoid danger of embolism. The incontinence in his case was due to laceration of the urethra during the first childbirth; the urine still dribbled notwithstanding six operations during the five years afterward striving to restore normal conditions. Semb (Norsk Mag. f. Lægevidenskaben, Nov., 1911).
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> Two cases of complete cure of hitherto intractable cases of incontinence of the urine in women. In the first patient, one injection of the ordinary commercial **paraffin** parallel to and along the urethra sufficed; in the second, three injections were necessary. E. H. Eising (Med. Rec., April 27, 1912).

The enuresis which occurs after labor as a result of prolonged pressure, traumatism, etc., usually subsides as resolution of the parts take place, and without treatment. In some cases, however, the enuresis not only persists but increases. A careful examination of the pelvic organs is then necessary and whatever morbid condition is found demands remedial procedures, often on surgical lines.

> The nature of the operation should depend upon the condition of the urethra and bladder neck. The **Frank operation**, combined with an anterior and posterior colporrhaphy in cases where there is a relaxed and gaping vagina, and some appropriate operation for retroversion where this exists, will cure the average case of incontinence coming on after labor, and of not too long standing. In cases where there is a marked dilatation of the urethra and of long standing or cases where from necrosis the muscular wall of the neck of the bladder and urethra are want-

ing, **Gersuny's operation** seems to offer the best hope of cure. Pawlik's and **Dudley's operations** have likewise given good results at the hands of their originators. G. Brown Miller (Surg., Gynec., and Obstet., Jan., 1910).

In 2 cases of incontinence of urine in women due to stretching or trauma of the urethra and surrounding tissue, in which numerous methods of cure had been tried without success, the writer obtained complete recovery by **cauterization** of the **internal** vesical **sphincter** through Caspar's operating cystoscope. Two or three deep grooves were burned in the sphincter at the point of transit from the bladder to the urethra. This causes scar-formation, and resulting contraction of the sphincter apparatus, which should in most cases be sufficient to produce complete continence, although in some conditions, as, for instance, where an extensive prolapse of the anterior vaginal wall is constantly pulling on the sphincter and stretching it, it probably would not be successful. The operation is easy of performance with the proper instrument, and free from danger. Caspar (Zeit. f. Urologie, II Beiheft, S. 238, 1912).

Kelly's Operation.—When incontinence of urine is due to damage to the sphincter during labor, the writer has devised the following operation, which has for its purpose to expose and bring together the torn or injured msucle fibers of the sphincter. "A mushroom catheter is passed into the bladder. With the index-finger resting on the anterior vaginal wall, it is easy to locate the exact position of the neck of the bladder. A longitudinal incision is now made in the anterior wall of the vagina about an inch in length, across the neck of the bladder. The walls of the vagina are next carefully dissected off from the urethra and from the bladder, and the dissection is extended up for half an inch or more on either side, embracing the neck of the bladder. Great pains are taken not to open the bladder or the urethra at any point. Not infrequently the dissection shows that the tissues of the bladder have been ruptured, leaving only the vesical mucosa and the vaginal walls intact. The next step is to take from two to three fine linen or silk sutures and pass them as mattress sutures through the sphincter ends and across the neck of the bladder from side to side, skipping over the central portion. When the first suture is passed the mushroom catheter is removed so as to avoid any difficulty in pulling it out when all of the sutures have been passed and tied. In case there is any doubt as to whether the muscles of the neck of the bladder have been drawn together, one or two more sutures may be applied above or below those already placed. It is sometimes so easy to demonstrate the thickened, rounded muscles at the neck of the bladder that they are then brought together in a very satisfactory manner. In other cases one simply has to grasp the thickened mass of tissue found just beyond the urethra and bring this snugly together from side to side." H. A. Kelly (Therap. Gaz., Oct. 5, 1912).

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EPHEMERAL FEVER. See Miliary Fever.

EPIDEMIC DROPSY. See Edema and Ascites.

EPIDEMIC STOMATITIS. See Mouth: Foot and Mouth Disease.

EPILEPSY (Morbus Sacer; Falling Sickness).

DEFINITION.—Epilepsy may be defined as a disease characterized by the habit of having convulsions, attended usually with unconsciousness, the seizures occurring suddenly and at irregular intervals, the subject showing an essential tendency to progressive mental and motor weakness.

VARIETIES.—The generic term epilepsy is applicable to and includes numerous subtypes, some of which differ from each other symptomatically and otherwise most markedly; hence the necessity for a classification of varieties. We have, for example, a division into two forms expressive of a difference in the degree and intensity of the motor spasm and impairment of consciousness in the attack—major and minor epilepsy, or, as the French express it, *grand* and *petit mal.* Other synonyms are general and partial, and, in a more restricted sense, frank or masked epilepsy. In *grand mal* both consciousness and motor spasm are involved in profound degrees. In *petit mal* both consciousness and motor spasm may be only slightly and transiently involved. In *general* epilepsy the motor spasm may involve all the muscles of the body and the loss of consciousness may be absolute. In *partial* epilepsy only one extremity or even one set of muscles may be affected and consciousness only slightly if at all perceptibly impaired.

Partial epilepsy is, perhaps, more readily recognizable under the name *Jacksonian,* or cortical, epilepsy: terms more popular, since they embody facts of etiological and pathogenic, as well as symptomatic, significance. The term "cortical" is, however, utterly indefensible here, since we have good reason to believe that all epilepsies are essentially of cortical origin. In *masked* (*larvated*) epilepsy there may be neither motor spasm nor apparent unconsciousness, but certain phenomena of abrupt onset in the psychical or motor volitional sphere may occur which, by reason of their habitual recurrence in the same or similar form, constitute a variety of the disease; automatic, causeless, but apparently purposive movements may represent the entire motor explosion. A transient stupidity or "absence of mind"—perhaps a random or irrelevant remark—may be the only evidence of impaired consciousness. Certain vasomotor disturbances, such as pallor, flushing, etc., usually accompany attacks of this character. In certain cases, first described by Weiss and to which he gave the name "psychical" epileptics, the explosion is, objectively at least, entirely in the direction of disturbed mental equilibrium, such patients being subject to irregularly and abruptly recurring paroxysms of transient insanity, usually with an aura, or warning, and with no recollection subsequently of the attacks. Such seizures, as well as other less-marked, but irregularly recurring psychical disturbances, are described by other writers as *epileptic psychical equivalents.* Special interest attaches to this subvariety of masked, or larvated, or psychic epilepsy, from a medicolegal standpoint, on account of the potentially criminal possibilities of such individuals during an attack.

The element of periodicity in the time of occurrence of the attack, a factor of some importance in both prognosis and treatment, has served as the basis for a chronological division into *diurnal,* or day, and *nocturnal,* or night, epilepsy, the former being still further divisible into the matutinal, or morning, and the vesperal, or evening, cases. In the succeeding paragraphs upon symptoms we shall find evidence of the necessity for a further elaboration of subtypes.

SYMPTOMS.—The symptom-picture in epilepsy varies quite widely, as has been intimated in the classification and description of subtypes. Not only is there a marked difference symptomatically in these clinical subvarieties, but each individual patient may differ in some major or minor particular from all others, although preserving in each instance some essential factor revealing a common identity. In typical *grand mal* the patient, with or without an aura or warning, is suddenly seized with a convulsion, attended with unconsciousness of greater or less degree. There is simultaneously a sudden alteration in color, either lividity or pallor, and the unconsciousness may be preceded or attended by an involuntary cry or scream. The patient falls unconscious regardless of surroundings; the muscles of the face and extremities become extended in rigid tonic, followed quickly by clonic spasm; frothy saliva, sometimes mixed with blood, escapes from the mouth; breathing becomes labored or stertorous from spasm of the respiratory muscles; the sphincters relax, allowing involuntary escape of urine, feces, and sometimes semen; the whole convulsive attack lasting from a few seconds to ten minutes or longer. This convulsion is followed, in typical cases, by a deep semicomatose sleep, lasting from a few minutes to several hours, the patient on awakening remembering nothing or very little of anything which occurred subsequent to the beginning of the convulsion.

> Analytical study of 306 cases of epilepsy. Only 14 per cent. were weak-minded. The seizures displayed a regularly ascending type in 61 per cent., an intermittent type in 26 per cent., and a descending type in 13 per cent. In 6 cases certain postepileptic symptoms were observed which have been previously regarded as premonitory phenomena. In 1 per cent. the epilepsy was reflex, from adenoid vegetations, and from masturbation in the same proportion. Syphilis was certain in only 1 of the 26 patients of over 30 years, and hereditary lues in none. Alcoholic parents were noted in 14 per cent., and 8 per cent. of all were addicted to the abuse of alcohol. Aura were noticed in 28 per cent. They usually precede the milder seizures. M. Biro (Deut. Zeit. f. Nervenh., xxiii, 1 and 2, 1903).

In atypical cases any one or several of these symptoms may be absent or so slight as to be scarcely noticeable. In some patients one or more of these symptoms may be replaced by substitutive conditions entirely different. In *grand mal* the postconvulsive somnolence may be replaced by an outburst of excitement or delirium or by states of altered personal identity in line with the theory of dual consciousness during which actions both embarrassing and reprehensible may be committed, involving sometimes grave questions of medicolegal responsibility.

In *petit mal* both motor spasm and unconsciousness are involved in far less degree, as the term indicates. Very often, indeed, the disturbance is of one sphere alone apparently, the attack consisting of a transient loss of consciousness alone, without motor spasm, or of motor spasm unattended with perceptible loss of consciousness.

Not only may the motor spasm occur alone; it may be further limited to one limb or to one set of muscles, or even to a single muscle. Such limited spasms are, however, observed —we have reason to believe—only in the organic epilepsies belonging to the Jacksonian, or so-called cortical, group. In such cases the limb or muscle involved points with localizing significance to the site of the disease-process in the corresponding center in the cortex. This statement is true, though of less value, as regards the various forms of sensory and psychical epilepsy. Among the rare clinical forms of atypical epilepsy most of which are of the petit-mal group are epilepsia procursiva, E. nutans, E. loquax, cardiac epilepsy, and migrainous epilepsy. *Epilepsia procursiva* is a form of the disease in which "the attacks consist in a straight or circling run, of a variable distance, which is rarely followed by a fall or cry, but by facial congestion" (Hare). The patient may run to the left or right or straight ahead. The act is essentially involuntary, of course, though absolute unconsciousness may not occur. This purposeless run may constitute the entire clinical phenomenon; it may represent the first stage of an ordinary epileptic attack; it may occur as a postepileptic phenomenon.

In *epilepsia nutans,* a minor form of Jacksonian epilepsy, the motor spasm is limited to the muscles of the neck, causing nodding of the head alone. In *epilepsia loquax* the attack consists in an explosion of speech, the focus of disease being presumably limited to the speech-center. I have seen personally only one case of epilepsia loquax among several thousand epileptics observed during the past twenty-five years. In cardiac epilepsy the attacks at first may resemble closely either angina pectoris or simple cardiac syncope. The patient has little more than an aura of precordial anxiety, usually at night, or when lying down with transient consciousness, but without motor spasm. There is in such cases either a bradycardia or a tachycardia, rarely a normal pulse, usually no organic cardiac disease, but often some arteriosclerosis.

> Attacks of tachycardia or bradycardia may last for hours, days, or weeks. After a variable interval the heart tends to become exhausted, and irregularity occurs—in short, heart block takes place. Stops are felt in the radial pulse, and concurrently nervous symptoms arise which vary from the slightest feelings of sparks flashing before the eyes or the waving of a sheet before the patient, to severe epileptiform convulsions, with loss of consciousness. Yet such attacks are most certainly not epileptic. From the writer's study of such cases he concludes that tachycardia is a pure neurosis, characterized by a great increase in auricular contractions from disturbed nervous influences. Clarke (Brit. Med. Jour., Aug. 10, 1907).
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> Five cases illustrating cardiac neuroses or cardiac epilepsy. In 1 case there were distinct spasms of angina pectoris. In 2 cases the angina succeeded the epileptic attacks, and there can be little doubt that they may have been due to the same cause. In a fourth case it seems quite likely that angina may come on later. One of the cases cited was remarkable for its persistent slow pulse. Newton (N. Y. Med. Jour., June 26, 1909).

It is at first a *petit mal.* Gradually, as a rule, the attacks become more severe, and finally may assume the major, or *grand mal,* type. This fact of transition in these milder forms to the severer forms of the disease is true of all cases as a possibility, although in many patients a *petit mal* remains such. The interchangeability as regards type is one of the many curious and inexplicable phenomena observed in this affection.

Migrainous epilepsy is a form of the disease in which habitual migraine may be either succeeded by true epilepsy of major or minor type or the epilepsy be succeeded by migraine, or the two conditions may alternate in the same patient. In some instances many phenomena of both diseases—if they be really two—may be noted simultaneously. I have seen two such instances.

> The frequent co-existence of epilepsy and migraine emphasized. Usually the epilepsy appears later than the migraine. One of the conditions, however, cannot be mistaken for the other. In instances where such a condition might have been possible it was seen that the migraine was a symptom only of the underlying epilepsy or the epilepsy appeared as a new element in addition to the migraine. It is not always easy to decide in atypical cases whether epilepsy or migraine is the main pathological condition. A neuropathic predisposition is always present in these cases, and frequently secondary etiological elements are present,—syphilis, alcohol, and other intoxications, injuries, arteriosclerosis, and excessive physical or mental efforts. Wilhelm Strohmayer (Münch. med. Woch., March 10, 1903).

In studying the peculiarities of attacks in individual examples of the disease it will be found of advantage to systematize such study under four divisions or stages: the preparoxysmal, the paroxysmal, the postparoxysmal, and the intraparoxysmal or intervalling period, as it is sometimes called.

The preparoxysmal, or pre-epileptic, stage covers the period immediately preceding the attack. By far the most important symptom to be investigated here is the aura, or warning, by which is meant some peculiar and constant subjective sensation or psychical impression realized by the patient as being premonitory of a fit. An aura is present in less than one-half of all cases, but it may be of great value and should always be carefully investigated. The aura may be referable to any of the senses. Flashes of light, sudden blindness, weird and fantastic visions, strange noises, tinnitus, deafness, numbness or tingling, or burning or pain in the extremities; disagreeable and indefinite, but constant stomachic sensations—as fullness, oppression, or pain; constriction of the throat, or of a limb, or of some part of the trunk—are among the auræ which have been noted.

The aura is an aid sometimes in deciding the etiological diagnosis. A sensation of coldness preceding an attack is said to be, especially if associated with subnormal temperature, almost diagnostic of cardiac epilepsy. A warning of precordial anxiety is also suggestive of this type. The aura often constitutes a guide to the location of the cerebral lesion, as, for example, in the patient reported by Beevor and Horsley, in whom an aura of a horrible taste and smell pointed to the uncinate and hippocampal gyri (see also Hughlings-Jackson), found to be the site of the causative lesion upon post-mortem examination. The interval between the aura and the attack varies. At times it is exceedingly short; in others the interval is sufficient to permit the patient to prepare for and prevent the attack. Other preparoxysmal warnings of an impending attack occasionally noted are headaches, vertigo, great irritability, stupidity, and quite frequently a ravenous appetite.

The irritability and impatience noted in many epileptic subjects is often supplemented by an excessive mobility of temperament. At one time depressed, hypochondriacal and convinced that he will never recover, at another the epileptic will show a sanguine and happy disposition. Often he is well satisfied with himself, and is fond of giving advice to others: at times he is cunning and jealous, and again he becomes unduly religious. It is the same with his actions: whilst sometimes prompt to carry out orders and willing to be of service, he is often dull, stupid, idle, and prone to refuse work. These characteristics are, however, neither limited to the epileptic nor necessarily to be found in every case, and a series of observations are recorded in some of which confirmed epileptics have shown a normal mentality, and in others the so-called epileptic character has been met with in feeble-minded or imbecile patients, and in cases of dementia precox and general paralysis. L. Marchand and H. Nonet (Revue de méd., Nov. 10, 1907).

The naughtiness, the moodiness and brutality shown by certain children who develop epilepsy later; he regards this abnormal behavior as an early manifestation of epilepsy. Another sign is attacks of excitement at times, the child speaking hurriedly, the syllables tripping over each other, sometimes actual stuttering; or the defect may manifest itself in apathy. Disturbances in co-ordination in children, an impulse to keep the arms, hands, or legs in motion, are defects observed in those inclined to epilepsy. Parents and teachers notice these defects before the physician sees the child, and they should be warned to be on the lookout for them as signs of a tendency to possible epilepsy. The earlier medical care can be given the child the better the outcome. Stadelmann (Med. Klinik, Dec. 25, 1910).

The paroxysmal stage should always, if possible, be studied personally, or through a competent trained observer or nurse. The statements of the patient are obviously unreliable. The most important phenomenon to be noted in this stage is the location of the first convulsive movement, or, as it is called, the signal symptom. This initial motor spasm, close in significance to the aura, is even more valuable at times in pointing toward the cerebral area involved by the lesion. Spasms, always beginning in the right foot, for example, point to the upper left Rolandic cortex, etc. The value of the signal symptom is greater the earlier it is recognized. Epilepsy of long standing, even though dependent upon a focal lesion, tends to become general. In old epileptics the signal symptom may actually appear to originate in the sound side, cortical irritability having become exhausted by prolonged insult of the originally affected hemisphere.

The postparoxysmal period is quite as important for the determination of essential facts as either of the other two and in much the same way. A monoplegia,—or limited sensory loss,—an aphasia, or an acute psychosis may possess an even more positive pathogenetic and localizing significance than the aura, or signal symptom.

Following one or more epileptic seizures of either type there may be a considerable period during which there are delusions of a more or less fleeting and temporary character. Such delusions are rarely fixed. They appear mostly in the form of accusations against attendants or fellow patients, charging the administration of poisons in the food or in medicines or abuse, resulting in the bruises, etc., which are really the result of falls. The mental disturbance is seldom of so severe a nature as to cause acts of violence, although acts of sexual perversion are not uncommon. Gradually the delusions disappear and the patient resumes his usual mental condition. W. H. Pritchard (Ohio State Med. Jour., March, 1910).

The interparoxysmal period is quite interestingly filled with curious phenomena in many cases. Various states of mental alteration or abnormality, of amnesia and morbid propensity, may appear, and may decide entirely the question of prognosis. It is this stage perhaps which is of most interest and importance in determining the medicolegal status of the criminal epileptic, although epileptic crimes of violence usually occur in the postconvulsive period. Evidences of essential degeneracy, manifest in stigmata, are conveniently considered here.

The psychoses of epilepsy have very definite and immediate associations with other manifestations of the disease. The plea of irresponsibility for criminal acts alleged to have been committed while an individual was suffering from epileptic mental alienation should be considered invalid, unless other and irrefragable manifestations of the disease can be adduced. The vague and ill-defined convulsions, which date back to infancy or early childhood, do not constitute such other manifestations. J. W. Courtney (Med. News, June 22, 1901).

The *paranoid* type of epileptic dementia is characterized by systematized delusions, ideas of persecution, loss of all the sentiments of affection, convulsive paroxysms, and attacks of violence, especially at the menstrual periods. The *catatonic* type is characterized by catatonic stupor, suggestibility, verbigeration, and negativism, which may go so far that the patient refuses to eat and has to be fed by gavage. The course is more rapid in this form than in any other.

Two theories as to the origin of epileptic dementia predominate: 1, that the dementia is due to the epilepsy, all the nervous phenomena of epilepsy are thought to be due to a cerebral irritation of toxic origin; 2, that the dementia is due to degeneration, traceable back to heredity. Voisin (Revue mém. des mal. de l'enfance, Aug., 1907).

Continuous partial epilepsy first described in 1894 by Kojewnikoff, is rare, only 16 cases having been reported. The essential characteristic of the disease is the co-existence in the same patient of attacks of epilepsy and partial convulsions persisting during the intervals between the attacks. In 11 of the 16 cases the patients were women. It was ascribed in 6 to infectious diseases, in 2 to syphilis, in 3 to alcoholism, and in 4 to traumatism. Little is known of the pathology, as no autopsy has as yet been secured, but Osokine removed a bit of the cortex during an operation on one patient and found very distinct changes therein. The disease develops very slowly, and the prognosis is unfavorable. It is liable to be confounded with paralysis agitans, chorea, tics, Jacksonian epilepsy, in which the paroxysms succeed each other without intermission, and finally epilepsy complicated by chorea. Schmiergeld (Presse méd., Sept. 26, 1908).

Asymmetry or abnormality of development, especially of the skull; undue elevation of the palate roof (Gothic arch), a deficient number of teeth, undue elongation or eversion of the coccyx,—the rudimentary tail of Féré,—are among the large number of stigmata observed.

There are characteristic functional stigmata in the voices of persons suffering from nervous and mental diseases. The characteristic speech of paresis and the thin, high-pitched voice of paralysis agitans are well known and readily recognized by all. Many of us have observed that there is something very peculiar and distinctive in the epileptic voice. The defect is shown in the expressionless quality of the latter; it renders the epileptic incapable of singing beautifully or speaking well. To one who has lived in a large colony for epileptics for several years the alteration of the epileptic voice is both striking and obvious. The writers have studied these changes. The method, used by them, is as follows: The patient speaks into a mouthpiece that covers his mouth rather tightly; this is connected to a small metal cup, the tambour. The top of the tambour is covered with thin rubber that yields to puffs of air and vibrations. A lever connected to the rubber receives the vibrations on a rapidly revolving smoked drum or kymograph. The arrangement can be conveniently called the "tambour method." In a list of 100 cases the writers were able to detect the disease in 75 per cent. of the cases by the voice sign alone. There is no precisely similar defect in any other nervous or mental disease. All types of epilepsy have been under study. One case had had but four epileptic fits and had never taken medicines for his disease. The voice sign seems to develop with the disease. The more severe the epilepsy and the longer duration it has, the more marked one finds the voice sign. The sign appears to depend upon the underlying brain degeneration, of which the epileptic fits are also an expression. The voice sign persists at least several years, even in the absence of fits, showing perhaps that even a prolonged absence of fits in epilepsy does not really indicate that a cure has been accomplished. The diagnostic and prognostic value of the epileptic voice sign is obvious. Clark and Scripture (Med. Record, Oct. 31, 1908).

DIAGNOSIS.—The recognition of epilepsy, in its typical form, is ordinarily a matter of no great difficulty. As, however, convulsions from uremia, dentition, etc., do not differ materially from epilepsy except in the matter of habitual repetition, it is necessary to consider all the collateral facts in addition to the seizure itself. A history of repeated convulsions of abrupt onset and without immediate assignable cause is, in itself, almost diagnostic. Even with such a history, however, the individual patient should always be given the benefit of a cautious differential examination, which should invariably include a careful uranalysis. Aside from the accidental or incidental convulsions which may accompany other diseases, such as nephritis, diabetes, certain forms of meningitis, brain tumors, etc., there are only four conditions which are likely to confuse the diagnosis: tetanus, malingering, syncope, and hysteria.

Tetanus differs from epilepsy in the two facts of retained consciousness and tonic spasm alone, clonic spasms being absent.

Malingering.—The detection of malingering will in some instances, as in the famous case of Clegg, the "dummy chucker," prove quite difficult. It is seldom the case, however, that a malingerer will learn his part as well as Clegg, and few of them will have the stoicism to withstand the tests of pinprick, hot iron, ammonia vapor, etc., which are indicated in suspected cases. I have more than once arrested the fit in a malingerer by firm pressure with the thumb against the exposed nerve at the supraorbital notch, and in one instance temporarily arrested the succession of fits in a status epilepticus. Clegg, by the way, was brought to an acknowledgment of malingering by being confronted with the fact that in his spasms he violated a physiological as well as a physical law, in that the thumb was contracted in flexion *outside* instead of *inside* the other fingers.

Syncope.—In simple syncope there is no motor spasm.

Hysteria is really a form of malingering, and the same tests apply. Here, as with other manifestations of hysteria, the disease-picture simulated is nearly always overdone. A strikingly constant physiological mistake of the hysterical is the reversal of the epileptic order of the convulsive movements, beginning with the clonic instead of the tonic, or mixing them up indiscriminately. If the patient happens to be a woman and of any of the Latin races (and I would add Polish Jews) it is necessary to exclude, with special and elaborate caution, major forms of hysteria. In many forms of minor epilepsy, especially in cases in which the disease manifests itself through the medium of psychical or sensory equivalents, a positive diagnosis is possible only after continued and close observation of the individual patient.

> Gowers attaches considerable importance to attacks resembling hysteria, which sometimes occur as sequelæ to epileptic seizures, especially of the mnor type. Certainly the association of epilepsy and hysteria in asylum practice is not uncommon, and doubtless many hysterical seizures of the most startling character would by more careful observation be found to have succeeded a minor epileptic attack. Contortions of the most violent nature accompanied by animal noises and attempts at biting, etc., are of not infrequent occurrence. In other cases patients pass into a dream state, which may resemble catalepsy or may more nearly approach the katatonic condition of dementia precox. W. H. Pritchard (Ohio State Med. Jour., March, 1910).

Cardiac epilepsy cannot, in its incipiency, in some cases, be differentiated from angina pectoris. The association of arteriosclerosis or other evidences of vascular degeneration, common to both conditions, adds to the confusion. True convulsions, too, have been noted in association with the Stokes-Adams syndrome. Epilepsy occurring only at night may exist for years unrecognized. Sleep-walking, night terrors, persistent nocturnal enuresis, and other similar phenomena should always suggest an inquiry as to the existence of epilepsy.

Syphilitic epilepsy may be recognized from the history of infection, together with a history of the symptoms, which are, with remarkable constancy, premonitory of syphilitic invasion of the brain. Unless the epilepsy develops in early or middle life, without other assignable cause,—the first convulsion having been preceded by periodically recurring headaches of evening onset and nocturnal exacerbation, associated with marked insomnia, or, less often, somnolence, with general malaise, and irritability of temperament,—the diagnosis of syphilis, as a source, should be rejected in spite of a history of infection. If this prodromal syndrome be present, it should be strongly entertained in spite of a denial of infection. The employment of the Noguchi or Wassermann test should be a routine procedure in suspected cases. The possibility of the convulsive form of paresis should never be overlooked, especially in patients developing convulsions in adult life.

> Eight cases, out of a large aggregate of colony material, in which

myoclonus occurred as a complication. In one case, a male aged 16, in which the epilepsy was due to fright, the myoclonus appeared as a complication of epilepsy about two and a half years later.

In another case in a girl aged 10, there was a history of certain crises which were more than myoclonic, which resembleed epilepsy and which seemed to be followed closely by myoclonic attacks of such severity that patient must lie abed. Under the observation period the patient had one or two attacks per month of epilepsy, which increased the violence of the myoclonus.

In a third case in a girl 3 years old, examination showed an idiotic child with extremities, head, and face in constant movement. Under observation the patient was seen to have myoclonic movements which led to general convulsions and unconsciousness. An attack of pneumonia temporarily checked both conditions, which reappeared with renewed severity during convalescence.

Eight cases in which myoclonus occurred as a complication of true epilepsy. G. Weiss (Kiel Dissert., 1905; Jour. Nerv. and Ment. Dis., March, 1907).

ETIOLOGY.—Heredity, age, sex, occupation, and the history of previous or coexisting disease, or injury, are all factors demanding investigation in determining the etiology in every case of epilepsy.

Heredity is remarkably common as an etiological factor, especially in idiopathic epilepsy.

The child is not simply a neuropath or a psychopath—he is a weakling. The constitutional weakness shows itself, as we often see, in the various stigmata of defective development and in general physical weakness—a weak digestion, a small thorax, a hypoplastic aorta, deficient circulation, poor teeth, slender frame, delicate muscles, undeveloped sexual organs, a small spinal cord, and the like. Given this constitutional weakness as a consequence of pathological changes in the germ plasma, various forms of nervous weakness may develop from extrinsic causes which determine whether the weakness shall be manifested in the nervous system, and if so, in what particular way it shall appear. Knapp (Boston Med. and Surg. Jour., Oct. 10, 1907).

A study of the pedigrees of 177 families containing epileptics showed the following facts: A great similarity of behavior in heredity, supporting the hypothesis that each is due to the absence of a protoplasmic factor which determines complete nervous development and that the nervous conditions named migraine, chorea, paralysis, and extreme nervousness behave as though due to a simplex condition of the protoplasmic factor which conditions complete nervous development, *i.e.,* persons belonging to these classes usually carry some wholly defective germ cells. Such persons may be called "tainted." When such a tainted individual is mated to a defective about one-half of the offspring are defective; when a simplex normal is mated with a defective about half the offspring are normal, the other defective or neurotic; when both parents are simplex in nervous development and "tainted" about one-quarter (actually 30 per cent.) are defective, and the proportion of tainted offspring is not noticeably higher when both parents show the same nervous defect. Normal parents which have epileptic offspring usually show gross nervous defect in their close relatives, and while we recognize that "epilepsy" is a complex, yet there is a classical type numerically so preponderant that, in the mass, "epilepsy" acts like a unit defect. Data point to a poisoning in slight degree of germ cells by alcohol, but the evidence is hardly crucial. There is evidence that in epileptic strains the proportion of epileptic children in the latest complete generation is double that the preceding. C. B. Davenport and D. F.

Weeks (Journal of Nerv. and Ment. Dis., Nov., 1911).

Heredity is variously estimated as present in from 15 to 50 per cent., Hamilton believing that it exists in one-half of all cases. It should be borne in mind, however, that he included immediate and collateral ancestral phthisis and apoplexy as evidences of heredity, which is not admitted by most clinicians. Epilepsy itself in the parent or grandparent or brother or sister is quite frequent. I have found parental epilepsy alone in 15 out of 77 cases. Many observers have found a much larger percentage. Insanity, migraine, alcoholism, consanguinity of parents, and major hysteria are among the more common ancestral taints observed. Migraine in the parent is, in my experience, far more frequent in the direct heredity of epileptics than is indicated in the literature. In Gowers's table of 1450 cases heredity appeared in the history of 36.6 per cent. As to age, epilepsy is peculiarly, though not exclusively, a disease of childhood and early life. Of Gowers's cases, 422 occurred under the age of 10 years, and 1087 under the age of 19 years.

According to the same table, females show a somewhat greater predisposition to the disease than males (females, 54.6 per cent.; males, 46.4). This relative difference is really greater than is indicated by these figures, if we take into consideration the greater exposure in males to cranial and other accidents, which are frequent causes of epilepsy. The occupation is often a sidelight upon the etiology. Epilepsy in sailors or prostitutes suggests syphilis; liquor-selling suggests alcoholism; painting and plumbing suggest lead as a cause.

Careful examination from the point of possible tuberculous taint, of 319 female epileptics at Salpêtrière. The writer found that not more than 20 (*i.e.,* 6.26 per cent.) of these could be regarded as tuberculous. The percentage of tuberculous subjects among the other patients was much greater—viz., almost 60 per cent. It would therefore appear that epileptics present a greater resistance to tuberculosis than other patients. M. Claude (La Clinique, Sept. 14, 1906).

In 33 out of 116 mentally backward children at the Frankfurt special school there were convulsions in early childhood,—that is, 28.5 per cent.,—while the proportion is still larger in certain other institutions of the kind. The etiological importance of syphilis in the epilepsy of adults is being recognized more and more; it is of the nature of a functional neurosis in these cases. The attacks occur at longer intervals, but the main difference from genuine epilepsy is the absence of deterioration of the mental faculties. In children with inherited syphilis, organic epilepsy may occur in any of its various forms. From one-third to one-half of all epileptics show some indication of the disease before they are 10 years old. Further research is needed, he says, on the subject of metabolic epilepsy; toxemia plays an important part in bringing on the attacks. H. Vogt (Archiv f. Kinderheilk, Bd. xlviii, Nu. 5-6, 1908).

Study of the pedigrees of 78 cases at the Monson State Hospital, and also those of allied families, making 90 pedigrees in all. The results are summed up as follows:—

1. We have no conclusive evidence that alcoholism in the parents is a cause of epilepsy in the children, although alcoholism is often associated with epilepsy. It may be regarded as a concomitant of epilepsy and an additional evidence of nervous weakness. 2. Feeble-mindedness is also associated with epilepsy, and there is some evidence that it is caused by the same defect that caused the epilepsy.

3. Fitting the material to the two hypotheses, first that epilepsy is a recessive trait that is inherited only as epilepsy, and second, that epilepsy, feeble-mindedness and insanity are due to the same defect which may appear in the form of any one of them, there is no striking evidence in favor of one to the exclusion of the other. The truth probably lies somewhere between the two. 4. While we are not in a position to say at present whether every case of epilepsy is inherited or to say in what proportion of cases it is inherited, we can say that in a large proportion of cases there is some nervous defect on both sides of the family.

These defects or stigmata may be epilepsy, feeble-mindedness, insanity, extreme nervousness, migraine, alcoholism, sexual immorality, and lack of moral sense. Flood and Collins (Amer. Jour. of Insanity, January 1913).

Certain diseases tend to develop an instability of the nervous system, and thus predispose the subject to the subsequent development of epilepsy.

The various forms of epilepsy, including that which appears to be of emotional origin alone, and the mixed varieties formerly classed as hystero-epilepsy, are the result of not one, but several co-existing factors, of varying relative importance and variously combined. Among these, however, three may be said to predominate: The cortical trouble, evidences of which may be detected even in emotional cases; the general toxic factor, usually of gastrointestinal origin; and circulatory instability, especially such as is manifested in sudden marked alterations of equilibrium in this system, which may be the result either of physical exertion or of emotion. In emotional epilepsy it is not the emotion itself which gives rise to the convulsive seizure, but the circulatory changes occurring in association with it. Jean Lépine (Lyon méd., Dec. 22, 1912).

Epidemic and sporadic cerebrospinal meningitis, insolation, scarlet fever, typhoid fever, and other kindred diseases, if attended with prolonged high temperature or toxemia, may lead to the development of epilepsy, the relationship being apparently one of cause and effect. A unique convulsion from any accidental cause may start the habit in a predisposed individual.

Case of epilepsy in a young man, occurring five months after a protracted convalescence from typhoid. Typhoid can easily produce the necessary lesions in the meninges, which may cicatrize and subsequently reopen after a very slight disturbance, a severe indigestion for example. Chalier and Juilhe (Presse méd., Sept. 30, 1911).

Case of a woman aged 27 years, who suffered from extreme constipation, sometimes not having her bowels moved for as long as a month. She had suffered from epilepsy for two years, the attacks occurring at intervals of about a fortnight. The writer performed Lane's operation of ileocolostomy. The result was a tendency to a too free action of the bowels at times, but since the operation there has been no return of the epileptic attacks. Cameron (Brit. Med. Jour., Oct. 14, 1911).

Disease of the heart or blood-vessels interfering with the circulation in the brain, and its nutrition, is properly regarded, we think, as a sufficient explanation of the etiology in certain cases of cardiac and so-called senile epilepsy, and perhaps in other obscure cases. With regard to the organic and toxic epilepsies, the etiology and pathology are those of the primary organic disease, the epilepsy in such cases appearing only as a single, though sometimes the most important, symptom. Any source of irritation within the cranial cavity, whether chemical or mechanical, may —though it by no means must—induce a convulsion.

> In the course of a prolonged and persistent asystole the alterations in the circulation of blood in the brain, the presence of toxic substances, and the vascular and inflammatory lesions in the brain combine to produce a hyperexcitability of the latter organ. This may express itself in crises of true epilepsy or of related psychic manifestations. F. Monisset and J. Gate (Revue de méd.; Med. Record, Sept. 7, 1912).

Of interest in connection with the subject of general predisposition to epilepsy are the statements of Peterson that the disease bears a ratio to the general population in this country of 1 to 500, and the further statement by Gray that a considerable majority of all epileptics have dark hair and eyes.

Reflex epilepsy, the existence of which is somewhat widely questioned, quite probably occurs, but in comparatively rare instances. Among the innumerable conditions of peripheral disease which have been noted as bearing an apparently causative relationship to the development of epilepsy are phimosis, adherent prepuce or clitoris, stenosis of the uterine os, nerve-cicatrices or surgical disease of the limbs or joints implicating nerve-trunks, carious teeth, eye-strain (esophoria, exophoria), obstructive disease of the nasal passages, aural disease, etc.

> Spratling's work on "Epilepsy and its Treatment" testifies unintentionally to the potent influence of eye-strain. If only 1 in 100 epileptics can be cured by relieving measures for eye-strain it would practically double the number of cures of epilepsy. The writer reports 4 cases in which fits appeared to be entirely suppressed for considerable periods by the correction of optical defects and also refers to two instances recorded by Dr. J. F. Crouch, of Baltimore. In some of these cases at least the temporary disuse of correcting glasses seemed to increase nervousness and to bring on a tendency of the original attacks. H. O. Reik (Jour. Amer. Med. Assoc., May 4, 1907).
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> At the Massachusetts Hospital for Epileptics, the writers placed on full mydriasis 88 patients to eliminate eye-strain and keep them with paralyzed accommodation for one month. They then compared the results as evidenced by the number of seizures with the number shown in other months. The following results were obtained: The total number of seizures in a minimum month was 545, or an average of 6.1 per patient. The total number of seizures shown in a maximum month with the same patients was 1630, or an average of 19.6 per patient. Adding the totals, this gives 2275 seizures, which, divided and averaged, give 13.2 per patient. The results as regards the seizures during the month of full mydriasis was 1110, giving an average of 12.6 seizures per patient, or approximately the same as that afforded by averaging the maximum and minimum months. While admitting that eye-strain may be an excitant in an individual of sufficiently unstable nervous system, the writers believe that the rôle played by ocular defects in the causation of epilepsy is very slight. Hodskins and Moore (Vt. Med. Monthly, March, 1908).
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> Case in which one month after correction of eye-strain, December, although the number of severe convulsive seizures increased somewhat, the total number fell from 404 to 157. In January the total number fell to 85, and in February to 7. Illness in the family during the spring of 1907, made necessary a change of residence for the boy. The journey to another

city and the far more irritating environment resulted in a slight increase in the number of seizures. With return to the old home and better conditions, during the summer, six weeks went by without a seizure. At the present time, March, 1908, six months have passed with but two or three slightest *petit mal*, hardly noticeable symptoms. G. M. Gould (Buffalo Med. Jour., May, 1908).

Case of a young man aged 23 who was subject to attacks resembling epilepsy, aggravated by the use of his eyes, which first appeared about a year and a half before he was seen by the physician. There was a premonitory cry, followed by a tonic convulsion, lasting from a quarter to half an hour. He was comparatively normal between the attacks. The attacks had become more frequent and had prevented him from following his occupation—that of a skilled mechanic. Close work requiring the use of his eyes and reading in the evening, had a tendency to bring on the attacks. Correction of the eye defect immediately was followed by cessation of the attacks, and he has been free from them for two and a half years. J. S. Wyler (Jour. Amer. Med. Assoc., June 8, 1912).

There is much to support the reflex theory in both experimental and clinical experience, although, as with many other phases of the subject, it is, as yet, no more than a theory.

Case of a healthy young man of 23 who became involved in a short circuit of the trolley wire, carrying a current of nearly 500 volts. Except for burns on his hands and transient pains in the abdomen he showed no ill effects of the accident, which had rendered him unconscious, until fourteen days later, when he had an epileptic seizure.

Similar seizures have returned since, every two weeks at least, and the young man's mind has shown slight impairment. Jolly (Münch. med. Woch., June 25, 1912).

Eight cases in which the epilepsy was due to reflex action from adenoid vegetations, their removal putting an end to the tendency. A reflex origin is far more common than generally suspected, and careful research for the source of the reflex would cure in many cases if this can be done before the condition has become so chronic that genuine epilepsy is installed. J. Tornai (Wiener klin. Woch., Oct. 3, 1912).

PATHOLOGY.—The true pathology of idiopathic epilepsy is as yet an unwritten chapter in the history of the disease. We have reason to believe that the essential location of the conditions causative of the explosions which constitute epilepsy is in some part of the brain cortex. The theory of interference with inhibition through irritation of the higher cells of the cortex, a theory elaborated *in extenso* by Hughlings-Jackson, is generally accepted, but not yet proved. This theory is not inconsistent with the experimental conclusions of Nothnagel, tending to establish the fact of the existence of a lower convulsive center in the floor of the fourth ventricle (pons).

The study of the morbid anatomy of epilepsy has so far been equally inconclusive. The abnormal conditions noted have varied with different observers, even with the vastly improved laboratory technique employed within recent years. The tuberous or hypertrophic sclerosis, found chiefly upon the convexity of the convolutions, by Barthez and Rilliet; the "gliosis" invading the normal cellular tissue, as described by Chaslin; the vacuolation of cortical cells with increase of spider-cells, found by Bevan Lewis; the hyperplasia of neurogliar tissue, with reduction in size and deformity of the cells, as observed by von Geison; these are all interesting and perhaps important; but numerous and insurmountable objections exist in each instance to their final acceptance.

> The writer carried out macroscopic and microscopic examinations of 20 brains of epileptic patients who had died in an insane asylum. The one outstanding pathological fact was that in epilepsy there was marked destruction of cortical nerve-cells and an overgrowth of neuroglia. The writer's own cases showed macroscopically an occasional gross lesion such as a cyst, a definable sclerosed area, etc. He found the sclerosis most marked in the hippocampus in 15 per cent. of his cases. Microscopically, he found a chronic atrophic condition of the nerve-cells preceded by chromatolysis. He saw no evidence of phagocytosis of the nerve-cells by leucocytes. As regards the nerve-fibers, he found them in much greater abundance in sections treated by Cajal's method than in those treated by Pal's method, showing that the myelin sheath disappears before the axone. The changes in the neuroglia did not especially affect the outer layer of the cortex, as has been asserted. All the changes were more marked according as the case was one suffering from a large number of fits or not. Changes in the vessels were not marked; small hemorrhages were seen in cases with severe fits. In older cases the vessels were dilated. The writer is unable to affirm that there is any special histopathological picture characteristic of epilepsy, but he considers epilepsy to be especially a disease of the cortex, having found only minor changes in the cerebellum, basal ganglia, medulla, and cervical ganglia. DeBuck (Le Névraxe, June, 1907).
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> Alzheimer found acute and chronic changes in 60 per cent. of all cases examined. In the nerve-cells the changes vary from slight degrees of chromatolysis to advanced atrophic degeneration. The extent of the change would seem to depend largely, if not entirely, upon the mode of death. Certain nerve-cells, showing well-marked excentration of the nucleus, which is usually of a globose character, are regarded as being typical of low-grade brains and to represent an embryonic type of nerve-cell. The vascular changes consist of dilatation and atrophy of the blood-vessel walls, perivascular infiltrations, and punctiform hemorrhages. The lymph-spaces are dilated and contain a foam-like exudate. Hyaline spheres or lobulated bodies are seen lying free in the lumen of the smaller vessels and capillaries, and sometimes large hyaline masses form casts of the vessels in which they lie. In neuroglia there is an increase of the glial tissue, especially that situated in the outer layers of the cortex, and of the cornu Ammonis. The meninges generally show slight fibroid thickening and a moderate leucocyte infiltration. Rupture of the vessels with extravasation of red blood-corpuscles and a delicate unorganized foam-like exudate are always present. The lesions found in the brains of epileptics are of wide distribution. The cerebellar membranes are often more affected than the cerebral. The glial changes are distributed unevenly over the whole surface of the cerebrum, but some regions are more especially involved—viz., the frontal and occipital regions, the cornu Ammonis, and the gyri around the fissure of Rolando. It is now generally accepted that such changes are the effects, and not the cause, of the seizures. Turner (Lancet, July 16, 1910).

Our knowledge as to the pathogeny of epilepsy is scarcely less obscure and no more satisfactory. Anemia or hyperemia in extreme degree may, either of them, excite a convulsion. This is a fact of experimental demonstration as well as of common clinical experience.

> The fundamental factor underlying both the ordinary faint and the epileptic fit is cerebral anemia. In the ordinary faint the cerebral circulation slowly diminishes *pari passu* with the falling blood-pressure. In the fit there is a sudden cessation of the circulation. Similarly the circulation slowly improves in the faint; in the fit it probably returns with greater rapidity. The fainting proclivity is commonly associated with other evidences of cardiac and vasomotor instability and an exciting cause is usually present. In epilepsy, the ordinary evidences of vasomotor instability are not so obvious and exciting causes are commonly absent. Russell (Lancet, April 3, 1909).

Mechanical irritation—as from trauma, neoplasm, or foreign bodies—is an agency capable of inducing convulsive attacks, as is well known.

Transmitted irritation from the periphery, through the medium of some local condition of disease,—as, for example, an injured nerve,—may excite a convulsive explosion of the corresponding cortical center. Carious teeth, stenosis of the uterine os, volvulus of the intestine, adherent prepuce, and many other conditions of local disease may, through the medium of transmitted irritation along the afferent nerve-trunks, provoke an explosion of the related cells of the cortex. Such cases constitute the much-questioned, but undeniably existent, class of reflex epilepsies. Finally, we have as a factor in the pathogenesis of epilepsy certain states of toxemia, some of them autogenous in origin, others depending upon the introduction from external sources of poisons with a relative affinity for the cortex.

The toxic epilepsies—those which are as yet positively determinable as such—are not numerous. There is reason to believe, however, that much more information remains to be gained as to the true pathogeny of epilepsy from the crucible and the chemist than from the scalpel and the anatomist.

> The metabolic findings in epileptics indicate that the disease is of toxemic origin in some cases. The brain and the skeleton are peculiarly sensitive to certain metabolic disturbances, to which epilepsy and rachitis should be referred. This suggests the possibility of more effectual treatment. The bromides have only a symptomatic action. Kauffmann (Münch. med. Woch., Nov. 10, 1908).

One of the most interesting phases of that most fascinating field of newer pathology,—perverted internal secretions,—and one which holds, I believe, great promise in the direction of enlightenment as to the pathogenesis of epilepsy, is today attracting much attention and experimental study. The thyroid, the pituitary, and the suprarenals are all being charged with etiological responsibility, through perversion of function, individually or collectively. Nothing approaching a *quod erat demonstrandum* has yet been attained, but I am one of those who believe that it is in this field of research that we shall find the answer to many of the hitherto unsolved mysteries of this, one of the oldest-known diseases in the annals of medicine.

> The dominant feature in the pathogenesis of the convulsions is impairment of metabolism, the spasmogenic agent being some toxic agent in the blood-stream. Pathological variations of vasomotor action, due more or less to a morbid condition of the blood, have also asserted themselves so strikingly in the production of fits that some observers have been inclined to regard them

as the foundation of the whole symptom-complex. Again, destruction of the spasmogenic agent has been urged by some as the only reasonable principle of cure in opposition to the use of bromides and chloral, which tend to increase its formation in the bloodstream. In a large proportion of cases the accumulation of these wastes is due to insufficiency of certain ductless glands, particularly the adrenals and thyroid. These organs, according to the writer, play an important rôle in the conversion of toxic wastes into benign and eliminable end products. Hence the beneficial influence of thyroid preparations in suitable cases. C. E. de M. Sajous (Monthly Cyclo. of Pract. Med., March and April, 1907).

Study of 17 epileptics to ascertain the relationship of the disease to the ductless glands. Of one fact the writers were assured, that in all cases of epilepsy the ductless glands show some modification of structure. These modifications are not of the same intensity in all cases, but in none were they found healthy. The thyroid is the most frequently affected. It is small and is usually sclerosed, but changes may occur in all its constituent tissues, connective tissue, epithelium, coloid substance and vessels. The condition of the parathyroid glands is not uniform. In the same subject one may be atrophied and sclerosed, another normal, and a third hypertrophied. The significance of these changes, in view of the present want of knowledge of their structure and function, is still uncertain. The pituitary and suprarenals did not present any constant change, though most of them were not healthy. The ovaries in most cases gave indications of functional insufficiency. The pancreas was normal in nearly all cases. Claude and Schmiergeld (L'Enceph., Jan., 1900).

It is conceded that the thyroid has a decided influence on the nervous system, especially the sympathetic. Concomitantly with the increase in size of the thyroid during pregnancy, functional nervous affections, such as neuralgias, chorea, and the various psychoses are prone to develop. The writer reports 7 cases in which epilepsy appeared in the presence of goiter, exophthalmic or simple, and which suggest, in conjunction with other evidence, a causative influence of the thyroid and other ductless glands on the development of certain cases of epilepsy. Even though all cases of epilepsy do not show thyroid changes, or all persons with goiters nervous symptoms, it is probable that the thyroid secretion in excess may act on the nervous system as do other toxines, or when deficient or perverted, may fail to neutralize certain toxins, occasioning epileptic attacks in susceptible individuals. Meyers (Monthly Cyclo. and Med. Bull., May, 1912).

The two predominating lines of advance in recent years are: the hereditariness of the disease, and disorders of metabolism due to perversion of the internal secretions of the ductless glands. Genuine epilepsy seems to be dependent upon certain unknown complex hereditary factors which bring about a form of cortical and subcortical instability. Upon this a variety of endogenous toxins may act to cause the disease. The fit is a manifestation of a reflex action of the disease, and as such should not be seriously interfered with by sedatives *per se*. As long as there is hope of bringing the real clinical pathogenesis under control, the use of sedatives is to be thoroughly discouraged. L. Pierce Clark (N. Y. State Jour. of Med., July, 1912).

PROGNOSIS.—The prognosis in epilepsy may be said to be progressively bad in a direct ratio with the number of attacks or the duration of the disease in the patient affected. If of long standing, the prognosis is bad, regardless of the cause. One convulsion, even though it be accidental, invites another, and, if repeated a few times, the convulsive habit is established and is curable only in rare instances.

> From 5 to 10 per cent. of all cases are curable. Emphasis laid on the necessity of a long-continued course of treatment, to extend over not less than two or three years. It should be carefully mapped out and executed to the letter, not only along one but many lines. Failure to secure good results in the treatment of epilepsy is usually due to a failure to treat the individual and his disease as a unit. The drug treatment alone, while invaluable in many cases and of some use in every case, often fails completely to meet the most important requirements. The prognosis in an individual case can only be given after observation extending over from six to nine months. W. P. Spratling (N. Y. Med. Jour., April 9, 1904).
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> Even severe and long-standing cases of idiopathic epilepsy are susceptible of arrest or cure. The majority of the permanent cures without drugs show a gradual subsidence of seizures instead of abrupt cessation. In patients treated with sedatives the criterion of cure must be somewhat modified, as a period of several months or even a year may be required for complete elimination of the drugs from the system.
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> The bromides do not aid the prognosis in epilepsy, especially as regards permanent cures. The writer has seen many cases treated with them steadily advance in physical, mental, and moral deterioration notwithstanding cessation of seizures. He uses bromides only, 1, as a therapeutic means of determining the severity of the disease, by ascertaining the sedative level necessary to hold the fits in check; 2, as adjuvants after all discoverable causes are set right and in such cases as need some small degree of sedation to bridge over certain periods. The seizures should no longer usurp the whole field of attention with their special therapy of sedation. Fully two-thirds of patients with "idiopathic" epilepsy show some functional anomaly of metabolism, either congenital or acquired; hence diet holds first place in the hygienic treatment. L. Pierce Clark (Arch. of Intern. Med., Jan., 1912).

Organic epilepsy dependent upon focal disease of even circumscribed limits is no exception to this rule, unless recognized promptly and treated properly by surgical procedure at once. Epilepsy due to syphilis, if promptly treated, can be cured; if treatment is delayed, it quickly becomes as intractable as any other form of the disease. This is true also of the toxic and reflex varieties. The element of heredity is of sinister significance in proportion to the intensity with which it may appear in the individual family history.

The age of onset is of importance, both as regards the curability of the disease and the development of serious complications. In epilepsy beginning in early childhood the tendency to the development of *status epilepticus,* a condition dangerous to life, is increased. I have seen this condition in 17 cases and in every one of them the disease began before the age of 10 years. The development of dementia is more probable the earlier the onset of epilepsy. Mania as a complication is more likely to be found in cases developing at puberty or later in life. Epilepsy developing without assignable cause at middle age (the *épilepsie tardive* of Forel) seems more amenable to treatment and the prognosis is rather better. In one such case, however, observed by the writer, the disease having developed after the age of 30, there being a history of parental syphilis, the patient died in an epileptic attack, the disease having persisted for several years.

Histories of 7 boys who all presented what seemed to be typical epilepsy and yet, after a time, improvement ensued so that a year or two to date has elapsed without further symptoms, although previously the seizures had been frequent. Even if the cure is not complete and permanent, yet this intermission of a year or so is a great gain for the mental development of the child. During the years the children were under observation there was nothing to shake the diagnosis of epilepsy. The patients are now from 9 to 18 years old. In another case a boy of 7 had two typical seiures with foam at the mouth, etc. He was vigorously purged and an ascaris was passed; during the two years since there has been nothing to suggest a tendency to epilepsy. Another boy of 5 has had no seizures for three years to date, although before that he had had convulsions several times a day after the age of 18 months; tetany had been diagnosed in this case. In another case a little girl had numerous attacks of sudden blank staring, dizziness, etc., with pavor nocturnus, suggesting a tendency to epilepsy, but these attacks gradually grew less frequent and there has been none for the last two years. The child is now 6 and is rather backward in school, but otherwise apparently normal. In 3 other cases the writer found that apparently typical epileptic seizures were the first manifestations of a severe progressive brain or meningeal disease; later the seizures gradually ceased. He believes that these 13 personal experiences of his justify the conclusion that the prognosis of epilepsy in children need not be inevitably unfavorable. Zappert (Jour. Amer. Med. Assoc., from Med. Klinik, Feb. 11, 1912).

Death from or during an epileptic seizure is not uncommon. The *status epilepticus* is especially dangerous to life. Paralysis of the cardiac or respiratory center is usually the immediate cause. Mechanical asphyxia is not infrequent. No reputable life-insurance company will accept an applicant known to be affected with epilepsy.

Death is imminent at the time of seizures, unless help is at hand. The cause may be traumatic, suffocation may take place, or death may occur without any apparent cause. Epileptics dying in a seizure will usually show some, but rarely if ever all, of the signs of seizure. The anatomical findings are edema and congestion, and often the diagnosis of seizure death has to be made largely by exclusion. It follows that the epileptic should be left by himself as little as possible. His walks should be in company or else in frequented places, and his repose should be under the watchful eye of a night nurse, or at least he should be in the same room with several other patients. J. F. Munson (Med. Record, Jan. 8, 1910).

The writer has collected 15 cases of sudden death during an epileptic fit, 13 from the writings of others, and 2 of his own experience; of these, 8 were due to cerebral lesions, bulbar hemorrhage twice, ventricular hemorrhage once, meningeal hemorrhage once, subpial hemorrhage twice, and cerebral congestion twice. Of the non-cerebral causes, he gives rupture of heart three times (left ventricle twice, right ventricle once), rupture of aorta twice, obstruction of respiratory apparatus by food twice. In the author's 2 cases (bulbar hemorrhage and subpial hemorrhage) the ruptured vessels were healthy. M. A. Collins (Alienist and Neurologist, Nov., 1911).

What constitutes a cure in epilepsy? Freedom from attacks for one, two, five, or even ten years cannot be considered as final evidence of cure, since it has been the personal experience of every neurologist to note recurrences after such intervals of remission. I have known a patient to exhibit a spontaneous remission for twenty-one years, the attack recurring without determinable new cause, and in exactly the same form, clinically, as at first. G. M. Hammond takes the position that relief from attacks for one or two years constitutes a cure, subsequent recurrences to be considered as new attacks. The objection to this teaching—there are many—is that, in some patients in whom the disease lasts through life, the attacks may be separated by intervals of a year or longer throughout the disease. Personally, I do not believe in the radical cure of epilepsy, if the disease has persisted for more than two years, except, perhaps, under an ideal environment attainable only in specially equipped institutions.

> The duration of life after the onset of the disease may be several years, but as the onset is very common in the early years of life, the net result is the premature death of epileptics as compared with normal people. The causes of death in epileptics are quite largely associated with the disease itself, and may be divided into two main groups, pulmonary conditions and conditions of purely epileptic character. Pulmonary conditions usually have at their foundation the pulmonary edema which is so often associated with seizures, etc., and hence are secondary to the epilepsy. Exposure while helpless or automatic after a seizure may be responsible for lung conditions. It is possible that the frequent congestions and edemas occurring in these lungs make the soil fertile for the tubercle bacillus. Munson (Med. Record, Jan. 8, 1910).

Of importance in estimating the prognosis is the presence or absence of stigmata of degeneration. Epileptics exhibiting cranial asymmetry or anomalies of development or well-marked intellectual or moral perversions are notoriously patients admitting only the most pessimistic prognosis. Well-marked periodicity in the occurrence of attacks in a subject constitutes a factor somewhat favorably modifying the prognosis.

MEDICAL TREATMENT.—The ideal treatment of idiopathic epilepsy is, in my opinion, attainable practically only through **institution environment**, organized on the colony plan, or as it is in Ohio or at Sonyea, New York.

The necessary regulation of the patient's habits, diet, clothing, exercise, sleep, and the employment of various adjuncts, direct and indirect, such as hydrotherapy and gymnastics, and appropriate culture of the mind and morals, can be accomplished systematically only in an institution established and conducted for such a purpose.

Where this is impossible, some such general plan as the following is advisable: Epileptics should be given some employment always, preferably physical and congenial and out-of-doors.

The **diet** should be regulated to two meals a day. Plain, wholesome food simply and properly cooked should be given liberally, but not in excess. Epileptics should be trained to eat slowly and to thoroughly masticate all food.

> Diet should be **very low in proteid.** The writer gives 125 Gm. (4 ounces) of bread, 16 Gm. (4 drams) of butter, and 250 c.c. (8 ounces) of milk as a rigid diet to be taken three times a day. This caused a reduction in number of seizures by 14 per cent. Rosanoff (Jour. Nerv. and Mental Dis., Dec., 1909).

The writer places his patients under a system of intensive training and dietetic regimen supervised by a "nurse-trainer" who lives with the patient on the same schedule and draws up daily detailed reports of his condition. The measures outlined for these cases include a **diet** consisting chiefly of cooked cereals, stewed fruit, milk, eggs, fish, and vegetables; calisthenic **exercises,** and a walk in the morning; periods of rest morning and afternoon; wood sawing or other useful occupation; **warm bath** and general **massage** in the evening; high **colon irrigations** every other night until colitis is reduced; **castor oil** or **calomel** every ten days. A daily uranalysis is made. Nearly every case with metabolic defect shows either indican or albumin for the first two or three months, later disappearing. All patients were found by the writer to benefit more or less permanently by this plan of treatment. He gives histories of 34 cases, including 29 in which the arrest of attacks had occurred from two to seventeen years before, and of a number of "cured" cases reported by other authors. **Bromides** are not advocated as a curative remedy, their **only** use being to **keep** the **fits in check.** They encourage the process of degeneration. L. Pierce Clark (Archives of Inter. Med., Jan., 1912).

We have a number of weapons at our disposal to combat the digestive intoxication and thus effectually eliminate one extremely important factor in the manifestations of epilepsy. The writer obtained excellent results from treatment on these principles in 37 cases. The main reliance is on a **diet** to avoid generation of intestinal poisons, thus discarding all foods of animal origin, including milk, eggs, fish, and meat. Milk and eggs are peculiarly liable, to generate the poisons and thus bring on the seizures, so he prohibits them entirely until the patient has outgrown the seizure habit. The diet should consist of vegetables, salads, fruits, raw and cooked, starches, honey and preserves, with sweet and diuretic drinks to a total of a liter a day. More fluid than this might have an injurious influence by raising the blood-pressure. The vegetable diet is supplemented by lactic ferments to transform the intestinal flora. None of his patients seemed to lose weight or suffer on this diet. DeFleury (Bull. de l'Acad. de Méd., Oct. 22, 1912).

Very little fluid should be allowed with meals. No special constant diet table is either necessary or advisable, except in individual patients in whom some special indication exists. The two meals should be given at 10 A.M. and 5 P.M. The patient should be required to drink water freely and at regular intervals between meals—as much as three or four pints should be taken daily. The living rooms should be light and never overheated or contaminated by impure air. Epileptics should be carefully protected from exposure to extremes of temperature. **Tonic baths** at proper intervals, keeping the skin active, and assisting in general nutrition are valuable, but there is no special system of hydrotherapy which will cure epilepsy.

As regards the drug treatment, we are still dependent upon the **bromides.** With regard to the use of the bromides in epilepsy I am firmly of the belief that **the curse of the epileptic** was the discovery that the bromine salts palliated and modified the disease. I have never seen a case of epilepsy *cured* by the bromides, and I do not believe that the theory of its use permits such a result. It modifies; it palliates; but it does not cure. The mode of use of the bromides is given below.

Antitoxins and various other sensational specifics, including hypnotism, have been vaunted in recent years, but have failed to stand the tests of trial fairly made.

As I have indicated under pathology, a field of experimental **organotherapy** in epilepsy has recently developed, which invites attention. Nothing of positive, demonstrated curative value has been established, but a rational basis for such experimentation has been laid, and much of promise appears as possible in this direction. The negative argument alone of abject helplessness in curative resources is in itself sufficient defense for this new departure. (See Animal Extracts.)

> The results obtained with **thyroid** treatment and the pathological changes in the thyroid not infrequently discovered tend to justify the separation from the "idiopathic" cases of the disease a group which may be designated as "thyroid epilepsy." In 2 of the author's cases in which bromides had proved useless, the administration of **thyroidine** brought about cessation of the seizures, an improved general condition, and an awakening of the mental and moral faculties, previously considerably obtunded. Thyroid treatment indicated, first of all, in epileptics with goiter or myxedema,—although even in these it will not always prove effective where abnormal thyroid functioning is not the sole cause, but is combined with various forms of intoxication or with disturbances of other ductless glands. Thyroid preparations should also be given in cases presenting merely some of the minor signs of hypothyroidism, such as edema, tendency to obstruction of the nasal passages, periods of aphonia, loss of lateral portions of the eyebrows, baldness, disturbances of temperature conditions or of the digestive functions, headache, somnolence, etc. Where thyroid preparations do good, bromides should be omitted. E. Gelna (Revue de méd., Jan., 1913).

The coal-tar derivatives—**antipyrin**, **phenacetin**, **lactophenin**, etc.—have also had their day, although their use is not altogether without benefit temporarily under certain circumstances.

Ethylene bromide, amylene hydrate, sulphonal, trional, curare, and solanum Cariolensis are a few among the hundreds of new remedies recommended which have proved of only slight value or useless altogether, or, as with amylene hydrate and curare, worse than useless. **Borax**, preferably in the form of the **biborate of soda**, is an exception in that it rarely does seem to possess a positive value, especially in nocturnal epilepsy. The dose is from 15 to 60 grains (1 to 4 Gm.) once, twice, or three times daily. Very much larger doses have been given and have been well borne. In this variety of epilepsy, too, the hypnotics —**sulphonal**, **trional**, **chloralamide**, and **urethane**—have a useful purpose as occasional temporary substitutes for the bromides.

In giving the bromides certain general facts should be recognized. The **potassium salt is the most effective.**

All **bromide salts** should be specially investigated as to purity of manufacture. Every dose of bromide should be given well diluted. The dose is inconstant necessarily and varies with the type and intensity of the disease in each patient. In an ordinary case, with attacks of moderate severity occurring four or five times a month, or less often, the patient should begin with 20-grain (1.3 Gm.) doses twice daily. This may be increased or diminished according to the effect. An insufficient dosage is practically useless; on the other hand, no unnecessary excess of the drug should be continuously introduced into the system, since bromism, if prolonged, induces a condition scarcely less deplorable than epilepsy.

If the attacks occur at more or less regular intervals, as at the menstrual epoch in women, such periods of attack should be anticipated by temporarily increased doses. Gowers's plan is quite effective in some cases, though bordering on the heroic. He gives one full dose of **potassium bromide** in the morning after breakfast in half a pint of water (250 c.c.), beginning with 2 drams (8 c.c.) every second morning, increased to 3 drams (12 c.c.) every third morning, and 4 or more drams (16 c.c.)—an ounce sometimes (30 c.c.)—every fifth day. The dose and order of interval are then reversed and the treatment is continued in this way for six weeks; small doses are then given for a year or more.

The writer cautions against exceeding from 15 to 20 grains (1 to 1.3 Gm.) a day, that amount being gradually arrived at. Five grains (0.3 Gm.) three times a day on scientific principles are of greater value than 20 grains (1.3 Gm.) three times a day without heed to eliminative precautions. Spratling (Albany Med. Annals, Feb., 1908).

Test of the effect of **open air** residence with appropriate occupation, but with entire exclusion of medical treatment or the use of any drugs, it having been asserted that this course would reduce the number of attacks and would probably effect a cure. The method of treatment previously followed, of giving the patients **sodium bromide** as salt with the food and excluding the use of common salt, was therefore suspended. The results show a great increase in the number of attacks, which again subsided on the restoration of the sodium bromide treatment. When the epileptics come under its full influence they become rather listless, stupid, and drowsy; that is the expected result, and a result to be attained; it indicates the point of saturation of the system by the salt, the point when the fits become controlled; the daily dose can then be diminished one-half, but not altogether discontinued. The drowsy, listless, symptoms soon pass off and the patient is again fit for work. Goyder (Brit. Med. Jour., Jan. 23, 1909).

The value of the **bromides** in epilepsy has been greatly overrated. The dosage commonly employed is not only excessive, but deleterious when its administration is prolonged. Small doses produce as good results as larger ones. Half of the favorable cases respond to treatment without any bromide being prescribed. When employed without ordering a **salt-free diet** the use of the bromides is almost valueless. Any decided amount of NaCl in the blood acts as an irritant to the cerebrum and increases the frequency and severity of the attacks. While it is not known why the exclusion of salt from the patient's diet is so beneficial in the treatment of epilepsy, it is known that equally brilliant results are obtained by its prohibition in chorea. Less than 10 per cent. of all cases of epilepsy are curable and only 50 per cent. of carefully selected cases were benefited by prolonged treatment. Wm. Lesem Amer. Med., April, 1909).

While the **bromides** do good in only a little over 50 per cent. of all cases, there is no substitute for these salts. In some cases, however, they augment the frequency or severity of the seizures, apart altogether from the toxic symptoms, or "bromism," which follow their prolonged or injudicious use. The dose usually given is too large, and it should be remembered that they have a cumulative property. A combination of **potassium bromide, picrotoxin,** and

antimony arsenate has been found of great use in arresting fits. W. A. Turner (N. Y. Med. Jour., April 30, 1910).

In some cases **bromide** abolishes the aura of the fit, and causes the patient to fall and injure himself in a way he did not do previously. In 2 cases with prolonged aura the writer has been able to avert fits for several months by simply giving a dose of bromide as soon as the aura is noted. In very many cases in which an immediate cessation of fits followed the exhibition of bromide its effect wears off, and the fits gradually begin to recur, and then a change of bromide will sometimes again cause a cessation of fits. He finds little difference in the two salts he has used principally, viz., **strontium** and **potassium,** except that from ½ to ⅔ dose of the potassium seems to have the same effect as the larger dose of strontium. Collins (Jour. of Mental Sci., Oct., 1911).

It is desirable to give just that amount of **bromide** which being **added grain by grain** on the return of attacks will finally prevent the occurrence of any attack. During this process of gradual increase you run against the occasional difficulty that effective doses, varying with the individual, may produce loss of memory, inertness, low spirits, and in rare cases forms of positive melancholia, maniacal excitement, and even suicidal or homicidal mania. You may play all the tricks you will, using arsenic, hot baths, and what not, and still you will sometimes be driven to conclude that a man had better have epilepsy than be overdrugged with bromides. Of course, where the attacks come at long intervals, this is the obvious course.

Although the **effects of bromide** on the skin are annoying, they may generally be **avoided** if the person will bear full doses of **arsenic and** use **hot baths.** There is, however, a small percentage of persons who are so susceptible to the bad effects of these drugs that a dose of a dram a day will within a week produce large rupia-like ulcerations, which so strongly resemble the rupia of syphilis that when the writer first saw and described them he was for a time completely deceived.

As you patiently add grain by grain to attain the restraining dose, so must you at the end of two years without attacks as slowly withdraw the drug grain by grain. S. Weir Mitchell (Therap. Gaz., March 15, 1912).

Potassium bromide seems to be curiously limited in its power for good in the treatment of epilepsy. Occasionally after having been effective for weeks or months or even years, its effectiveness will, without assignable cause, cease. This is true not only of potassium bromide, but of nearly, if not every, other drug useful in epilepsy. Some other salt of **bromide,** or several of them in combination (**sodium, strontium, ammonium, lithium,** are valuable in the order mentioned), or one or two of the bromides in solution with **antipyrin** or in combination with **phenacetin** may be advantageously substituted for the single salt.

Strontium bromide, as a rule, acts better in controlling the number and severity of the fits than the mixed bromides of sodium and potassium. Strontium bromide rarely caused depression and rashes remained absent in all the writer's cases. This remedy, in the author's opinion, acted best and most consistently on the female patients, in all of whom the action, as regards controlling the fits, was superior to that of the mixed bromides.

The maniacal symptoms of the male patients while taking strontium bromide were not influenced to any perceptible degree. The mental condition of the female patients appeared to improve. J. M. Bennion (Lancet, Jan. 5, 1907).

The writer prefers a mixture of the three bromides, sodium, potassium, and ammonium, to which he adds in some cases **calcium bromide**. The dose must be carried up to a point at which the motor manifestations are controlled without marked bromism, and must then be kept at that point for months or years. Irregularity and lowering of the dose without permission is responsible for most of the failures. A great aid to the effect of the treatment is given by **restricting** the amount of **chloride of sodium** that is used with the food to a small quantity. The bromide is then effective in smaller doses. It should be continued three years after the last attack. Paul Boncom (Prog. méd., March 19, 1910).

The **bromide** of **strontium** given in large doses does more effectually control the atacks of epilepsy than the usual bromides, and is more often followed by recovery. To effect this result the treatment must be persisted in over an extended time; in many cases ten to twelve months' treatment is necessary, and in a few cases even a few months longer. Those which most readily yield a good result are the young adults who have not for an extended period suffered from attacks, but even in middle-aged patients success is usually attained by persistent administration of the drug. M. R. Callender (Lancet, June 15, 1912).

A diet low in salt, *i.e.,* poor in chlorine, has been found to increase the efficiency of the bromides, thus making it possible to administer smaller doses of the latter.

The beneficial effects of a **diet** which is arranged so as to be poor in chlorine, upon epileptic patients, who are at the same time on the **bromide** treatment, were first brought to light by Toulouse and Richet. André Viteman, in 1906, published a remarkable work on the chemical elimination of chlorine, of bromine, and of other substances, both by the kidneys and into the cephalorachidian fluid. He demonstrated that a rigid **dechlorinized diet** combined with the **bromide** treatment (2 Gm. or 30 grains, in twenty-four hours) in an epileptic, will yield the following modifications: The urea and the phosphates in the urine are eliminated in much larger quantity, and, on the contrary, the proportion of bromide is lowered. In the organism deprived of chlorine there occurs therefore a retention of the bromides, when a moderate dose of this salt is administered. Elimination does not commence until after the saturation of the organism by the salt, and this depends both on the quantity given and the weight of the individual. Among 16 cases, Viteman found albuminuria in 6 (in one as much as 0.30 per cent.), which he thought might fairly be imputed to the undue prolongation of the treatment. (Journal des Praticiens; N. Y. Med. Jour., Aug. 17, 1907.)

Results in 15 cases of epilepsy treated by a diet low in salt in combination with the **bromide** treatment. These patients were observed continuously for a period of five years, and the improvement has been constantly maintained. Immediate improvement followed the **withdrawal of sodium chloride from the diet.** In 6 cases the attacks ceased completely; in the other 9 there was marked improvement. The convulsions not only disappeared, but the mental conditions of the patients improved, and in no case was any marked mental deterioration observed which is so common in epileptics treated with bromides. Ulrich (Münch. med. Woch., Bd. lix, S. 1947, 2007, 1912).

Sometimes the addition of one of the motor depressants—as **hyoscyamus, conium, belladonna,** or their alkaloids—is quite as effective, at least temporarily. As a matter of further curious interest it has been proved by experience that in such cases a change to almost any new drug will result in temporary improvement—a fact which explains, in part at least, the almost limitless pharmacopeia of the disease.

The use of opium, reintroduced recently by Flechsig, is deserving of mention and a limited commendation. Flechsig's method consists in the daily administration of **opium** in the form of the solid extract in doses gradually increased up to several grains (12 to 15) daily, five or six weeks usually being required. Treatment by bromide is then substituted for the **opium.** This treatment is of distinct benefit in old, long-standing, idiopathic epilepsies which have not been benefited by the bromides. It is contraindicated in recent epilepsies and in the organic cases.

> **Chloretone** used in 12 obstinate cases and recommended where bromides fail. All cases showed marked reduction, and in 1 cessation of attacks. It is best given in glycerin solution. In the robust 10 grains (0.65 Gm.) may be given *t. i. d.* Sometimes "chloretonism" symptoms appear: Increasing dullness and drowsiness, later vertigo, irritability, pallor of mucous membranes, sluggish reflexes, albuminuria, and an eruption. The urine should be examined daily and the drug stopped if albuminuria or other symptoms appear. The benefit from chloretone usually persists a month after discontinuance. Bentley (Austral. Med. Gaz., March 20, 1911).

Four remedies are deserving of special mention in connection with special forms of epilepsy for the relief of which they seem especially efficacious: **nitrite of amyl** and **monobromated camphor** in cases of *petit mal,* **duboisin** in hysteroepilepsy, and the **hydrobromate of coniine** in the *status epilepticus.* Nitrite of amyl also possesses value as a drug which, if used promptly in cases preceded by an aura, will often prevent the further development of the attack. **Chloroform by inhalations** is at times temporarily useful in controlling the *status epilepticus.*

> Clonic spasms can be suppressed and the consciousness restored by **placing the epileptic on his left side during the tonic period.** This method of arresting the seizure was first successful by McConaghey, of Edinburgh, and the author has found it successful in every instance in which it has been applied. Crocq (Fourteenth French Congress of Neurol. and Psych.; Semaine méd., vol. xxiv, No. 32, 1904).

I have found the use of **cardiac tonics** of positive value in combination with the bromides in what is known as cardiac epilepsy. The condition of the heart and pulse is the guide to the selection of the adjuvant drug.

> The best treatment of epilepsy is to put the system in such a condition that excitants to epileptic attacks, such as autointoxications from the gastrointestinal tract, from fatigue, from poisonous products, which should be eliminated from the body, will not develop within the body, and also to guard against those experiences which we have learned often precipitate attacks. Also so to influence neuromotor irritability in a sedative way that discharge of energy in the shape of explosion will be less likely to occur.
>
> As to the neurasthenic phenomena, the writer finds that their treatment by **rest, exercise, change of environment, isolation, hydriatics, massage, diet,** avoidance of deleterious indulgences, and conformation to hygienic rule is so far superior to drug-therapy that he rarely uses drugs in these cases, unless to fulfill some pointed indication. Joseph Collins (Med. News, July 5, 1902).

To a certain extent, though far more limited than one would suppose from *a priori* reasoning, the etiology affords a basis for treatment. **Anti-syphilitic treatment** should be at least given an energetic trial, as epilepsy is due primarily to syphilis. Such patients, however, as a matter of fact, are not often cured by this means, and as a further fact of interest it will be found that such patients do not bear well energetic specific treatment. Various toxic agencies or conditions of visceral disease, standing in a presumably causative relationship, should be treated, of course, but cure of the toxemia or the visceral disease very rarely results in cure of the epilepsy.

A course of **Carlsbad waters** for gastrointestinal disturbances seemed to have a favorable influence on long-existing epilepsy. The results were so good that the writer urges prescribing a course at Carlsbad as a routine measure for certain patients with epilepsy, especially those in whom migraine accompanies or substitutes the epileptic seizures or those with some metabolic disturbances, uric acid diathesis with oxalate stones in the urine and pain in the joints and limbs. It was in such cases that the results were most striking. Biernacker (Wiener klin. Woch., March 17, 1910).

Veronal in small doses is often a more efficient drug than the bromides. The writer gives it during the intermissions in doses of 0.1 to 0.3 Gm. (1½ to 5 grains) from twice a day to twice a week, depending upon the age and the severity of the case. A cumulative effect or intoxication was not observed. Liebl (Med. Klinik, Nu. 45, 1909).

Having operated on a young epileptic for inguinal hernia under **spinal anesthesia,** the writer was surprised to learn, two years later, that the young man had had no seizures, although previously they had recurred at intervals of ten or fifteen days during the preceding nine years. The writer then applied spinal anesthesia systematically in treatment of epileptics and reports great improvement in every instance. He urges others to give this method a trial as his experience in this line is limited, having had only 4 epileptics in his charge. G. Giacomelli (Gaz. degli Osped., Jan. 18, 1912).

(1) Secure bowel movements once or twice daily. (2) Have patient drink **water** freely. (3) Tepid **sponge bathing** or brief immersion **baths** followed by gentle rubbing. (4) Mild **exercise in open air..** (5) Mixed **diet,** consisting of vegetables and milk in liberal amount, and also white meats; starchy foods in limited quantity; normal amount of fats. Correct digestive difficulties. (6) **Bromides** to be used early in disease and in sufficient amount to control seizures. (7) **Sodium chloride withdrawal** found an aid to bromides, though prohibition of salt should not be so radical as to cause anorexia and loss of weight. (8) Combination of **sodium glycerophosphate** with bromides proves beneficial. (9) **Thyroid extract** valuable in epileptic children with arrest of developmeent, as well as, occasionally, in other cases; to be given persistently, in small doses; after a time, it will be found bromides can be reduced or even for a while suspended. (10) Trial of **pituitrin** in epilepsy justifiable. (11) Symptoms preliminary to seiures, such as headache, depression, etc., indicate the prophylactic use of a **saline purge, diminution of food,** and increaseed bromide dosage. Dercum (Therap. Gaz., March, 1912).

The frequently demonstrated fact that the coagulability of the blood was reduced in epilepsy suggested the use of calcium, the most satisfactory salt of which is **calcium lactate.** From 5 to 15 grains (0.3 to 1 Gm.) may be given three times daily.

The writer gave **calcium carbonate** twice daily in the form of a cachet containing 10 gr. (0.6 Gm.) and found it of real service. His experiments dealt with 5 epileptics, and extended over two years. His object was to determine (1) how far the treatment diminished the number of fits occurring per diem, and (2) how far it improved the mental condition of the patients. He alternated periods of two to four months during which calcium carbonate was given with similar periods during which expectant treatment was adopted. The daily average of fits was considerably lessened while the salt was taken. A very great improvement occurred in the mental and physical conditions of the patients; and they were less confused, irritable, and excitable while taking the calcium carbonate. D. Linguerri (Bull. d. sci. méd., Dec., 1906).

The writer has successfully used **calcium lactate** in the treatment of epilepsy. All his patients have improved, some more so than others. The usual dose was 15 grains (1 Gm.) of calcium lactate, three times a day. Littlejohn (Lancet, May 15, 1909).

In 29 cases of epilepsy **lime** had a pronounced effect in mitigating the seizures and reducing their number. The lime salts are preferable to the bromides at times, the best results being obtained when a course of lime was alternated with the ordinary bromide treatment. From 2 to 3 Gm. (30 to 45 grains) of **calcium hypophosphate** in fractional dose were given daily. The patients were all chronic epileptics, although the affection was of traumatic origin in some and associated with infantile spastic paralysis in others; the majority, however, were of the idiopathic variety. F. Ciccarelli (Policlinico, Feb. 7, 1909).

Crotalin, or rattlesnake venom, has recently been introduced, but without careful animal experimentation to determine its immediate or remote effects. The danger of anaphylaxis, pending such analytical work, renders the use of this extremely toxic agent somewhat hazardous.

Series of 36 cases, between the ages of 5 and 62 years, were treated with **crotalin.** All were average cases. That form of the disease most influenced by the venom solution was the idiopathic or genuine epilepsy. The improvement in the mental condition of the patients was marked, while the frequency of epileptic attacks was greatly diminished. The character of the convulsions was also modified. It was observed that patients who had formerly had from 2 to 8 attacks per week, had none for periods ranging from four mouths to two years. Others who had formerly been subject to 1 or 2 major attacks a week, experienced, after treatment, only minor attacks, and these two or three weeks apart. In regard to the dose, the writer recommends starting with 1/200 grain (0.0003 Gm.) and gradually increasing the strength according to the individual case. Patients vary greatly as to the swelling, erythema, and cellulitis produced by injection of the venom solution. The effect often varies, even in the same individual, 1/100 grain (0.0006 Gm.) sometimes causing more severe local reaction than 1/50 grain (0.001 Gm.). R. H. Spangler (N. Y. Med. Jour., Sept. 9, 1911).

The treatment of epilepsy with **crotalin**, *i.e.*, the sterile, dilute virus of the rattlesnake, *Crotalus adamanteus*, was tried by the writer with very satisfactory results, although the time elapsed does not warrant a final judgment upon its value. Fachenheim (Münch. med. Woch., Aug. 29, 1911).

SURGICAL TREATMENT.—**Intracranial surgery** is limited to those cases recognizable positively as dependent upon an organic lesion of limited extent and surgically accessible, the location of the explosive focus being determinable at least approximately from the symptoms.

> A series of 56 personal operations showed that it was justifiable: (*a*) In traumatic epilepsy with external evidence of injury; (*b*) *do.*, without evidence of injury when nature of attacks or symptoms immediately following injury indicates seat of lesion; (*c*) in Jacksonian epilepsy; (*d*) in general epilepsy where suggestion of a focal lesion may be found before or after attacks in some disturbance of motion, sensation, or reflexes. Gratifying results may be anticipated after operation in 10 to 25 per cent. of cases. Frazier (Therap. Gaz., March, 1912).

To the above class of cases may oe added that small number included in the etiological variety known as reflex epilepsies. In organic epilepsies the results of surgical treatment depend upon the accuracy and promptness of diagnosis, including localization chiefly, and secondarily upon the promptness with which surgical interference is adopted, and the personal skill and surgical judgment of the operator. Shock and hemorrhage are practically the only immediate sources of danger, asepsis having eliminated other surgical complications. Both shock and hemorrhage are avoidable or can at least be reduced to a minimum which does not endanger life. Wyeth's method of accomplishing this result in intracranial operations by dividing the operation of entrance into two or more surgical *séances* upon succeeding days is eminently satisfactory. So safe, indeed, is this method as to have rendered perfectly legitimate surgical entrance of the skull for purely exploratory purposes.

> Surgical treatment of epilepsy is indicated in cases which prove intractable to general medical and hygienic treatment, and these, unless the disease be somehow arrested, will soon terminate in imbecility and death. In such cases the affected motor area is covered by more or less edema of the pia-arachnoid and this edema probably so affects the cells of the cortex as to predispose to or cause the epilepsy and imbecility. We can, by the operation of fenestration of the dura mater, drain these edematous areas and prevent reaccumulations. By the operation the progress of the disease has always been retarded in the 20 cases operated, while in several the fits ceased. Alexander (Lancet, Sept. 30, 1911).
>
> During the last ten years the writer has operated upon 106 cases of genuine generalized epilepsy after the method of Kocher, and investigation of all these cases has only recently been carried out. Of 58 cases on which operation was done upward of five years, 8 have ben completely cured, 15 have been decidedly benefited, while 33 have not been benefited. Ito (Deut. Zeitsch. f. Chir., Bd. cvx, H. 5-6, 1912).

The technique of the operative procedure varies with each case appropriate for operation, as well as in accordance with the surgical peculiarities of the operator. There is a growing pessimism representing the return swing of the optimistic pendulum of ten years ago with regard to the value in results of surgical treatment for organic epilepsy. Von Bergmann and McCosh, among recent writers, unite in a demand for greater conservatism. Mason, quoted by Gray, tabulates 44 cases treated surgically, with 2 recoveries, or about 4½ per cent. This table is capable of another interpretation, however, which is decidedly more favorable from the fact that, in more than half, the cases in which the time of observation after operation is said to have been "insufficient to confirm the claim of cure," further lapse of time may serve to establish the claim at least in some of these cases.

Exploratory trephining is advised in traumatic epilepsy. In 11 cases operated by the writer, 4 of idiopathic and 7 of surgical epilepsy, cysts were found in 2 instances, cicatrices in 4, and edema of the pia in all. Improvement resulted in all the cases from removal of edematous fluid. The epileptic attacks returned in 4 cases. Tilmann (Münch. med. Woch., Nu. 32, 1909).

The patient and his relatives should be impressed with the fact that when he has undergone an operation for epilepsy, postoperative supervision is necessary. Surgery may put him in line for a cure, but alone it often fails where it should not, because of the too great solicitude of an anxious mother, a foolhardy persistence of the patient in forbidden paths, or the want of a distinct and intelligent guide to direct the whole aftercourse.

There can be little question about the correctness of the plan for excision of the brain centers of those muscles or muscle groups which habitually are affected at the beginning of the seizures, although it is not directed toward the foundation of the trouble in the sensory centers through whose perverted activity the fits are awakened. Bryain (So. Med. Jour., May, 1912).

In the past there has been much ill-advised and indiscriminate operative intervention in the epilepsies, and some of the cases, viewed either from the purely surgical point of view or from the standpoint of the epileptologist, are sad commentaries on the ill-judged activity of the surgeon. The writer reports 19 cases in which some surgical intervention was undertaken on the head, and which afterward came to autopsy. In some cases, the scar-tissue formation has been the evident cause of continued irritation and in others there was cerebral destruction which was sufficient to cause the attack, but in others there was apparently both a successful operation and an absence of lesion. The reason for this ill success is that there was a decided neuropathic taint in many of the family histories, which the operation does not remove. Again, some patients who desire operation have alcoholism or venereal excesses as part of their etiological equation. There again the knife is handicapped. In some of the traumatic cases the trauma is not the cause, but is the result, of the first seizure, and therefore the operation fails to remove the original cause. Munson (N. Y. State Jour. of Med., Nov., 1912).

Of the total number of 3502 patients admitted to the Craig Colony for Epileptics, 48 had been trephined either before admission or during their treatment at the Colony. In a few of these the operation had been repeated. Naturally, none of the patients operated on at the Craig Colony have been trephined immediately after a trauma or the onset of the epilepsy, as they were all confirmed epileptics at the time of admission. The results of operation on these patients cannot be compared with those obtained by operation immediately after the trauma or in the early stages of the epilepsy. None of the patients trephined at the Colony have been permanently relieved from the attacks, although most of them were benefited, at least temporarily, by the operation. In several cases in which operation was done before admission, the condition of the patient had been made worse by the operation. Sharp (N. Y. State Jour. of Med., Nov., 1912).

Almost all cases of epilepsy which come within the etiological subtype "reflex" demand surgical measures of relief, the removal of the peripheral course requiring, in most instances, the knife. Phimosis, cervical stenosis, carious teeth, nerve-cicatrices, diseases of the bones, eye-strain, and ovarian disease are all conditions for which the knife or other surgical or mechanical agents are indicated.

In all cases of epilepsy, when such conditions or any one of them exist, either coincidently, alone, or as the presumable cause, they should be appropriately relieved. It will not always, nor indeed often, cure epilepsy; but such conditions undoubtedly aggravate the epileptic tendency, and should be eliminated. I have never yet seen a case of epilepsy cured or even benefited permanently by operations upon the eye-muscles or by removal of the ovaries, and I have seen scores of patients upon whom such operations have been done.

Such operations should be done, though with discrimination and always with the frank acknowledgment to the patient of the uncertainty of results.

William Broaddus Pritchard,
New York.

EPINEPHRIN. See Animal Extracts.

EPISPADIAS. See Urinary and Genital Systems.

EPISTAXIS. — DEFINITION. — Epistaxis is nasal hemorrhage, or bleeding from the interior of the nose. While the great majority of cases have their origin from some spot situated in the anterior part of the septum, the bleeding may take place from any portion of the mucous membrane.

[The arterial supply of the interior of the nose is derived from the ophthalmic and the internal maxillary branches of the internal carotid artery, and from the superior coronary artery, which is a remote twig of the external carotid. The ophthalmic artery divides into numerous branches, the anterior ethmoidal accompanying the nasal nerve through the anterior ethmoid foramen and supplying the anterior ethmoid cells, the frontal sinus, and also gives off other nasal branches, which are distributed similarly to those derived from the posterior ethmoid artery. The posterior ethmoid has its origin just as the ophthalmic artery approaches the inner wall of the orbit. It passes through the posterior foramen in the ethmoid bone, supplying the posterior ethmoid cells and giving off nasal branches, which descend through the cribriform plate, and which are spread over the upper and outer wall of the nose.

The internal maxillary gives off the nasopalatine, the infraorbital, and the alveolar arteries. The nasopalatine is the most important of these branches and enters the nasal fossa at the posterior portion of the superior meatus, and divides into an internal and an external branch, the former passing obliquely downward and forward, supplying the mucous membrane covering the septum, and finally anastomosing with the descending palatine artery. The blood-supply to the nose proper from the infraorbital and the alveolar arteries is rather meager and pertains more particularly to the antrum of Highmore.

The inferior artery of the septum is a branch of the superior coronary, and supplies the anterior portion of the septum; hence it is frequently held responsible for many cases of epistaxis from the so-called "hemorrhagic area" of the nose, or Kresselbach's spot, situated on the septum near the tip. R. B. Scarlett.]

ETIOLOGY.—1. *Traumatism.*—One of the most frequent causes of bleeding from the nose is injury of some sort. A blow upon this organ produces a rupture of the smaller blood-vessels in the mucous membrane and permits a free flow of blood until checked. This may also result from violently blowing the nose. The pernicious habit of picking the nose is not infrequently the causative factor. Foreign bodies inhaled with the atmosphere and impinging against the vascular area, more directly exposed to such injury by an anterior deviation of the septum, or their insertion by the patient, frequently predispose to hemorrhage. Postoperative bleeding is usually mild in degree and is seldom difficult to control. Bleeding from the nasal cavities following traumatism is particularly significant if fracture of the perpendicular plate of the ethmoid is determined, for this bone is usually involved in fractures of the anterior fossa of the skull. In such cases injury to the ophthalmic artery or its branches takes place.

2. *Diseases.*—Several diseases of a local nature may be responsible for bleeding from the nose. A catarrhal inflammation produces a chronic hyperemia of the mucous membrane, and the increased blood-supply resulting therefrom contributes to epistaxis. The veins in the anterior portion of the septum may be varicosed, or the effort to remove scabs, especially in atrophic rhinitis, may produce the same result. Adenoids in children, or a septal ulcer in a patient more advanced in years, is sometimes the contributing agency. One of the diagnostic signs of malignancy of the nasal chambers is the tendency for the tumor to bleed; however, some of the new growths of a benign nature may produce the same symptom, as has been noted in cases of nasal polypi. In the malignant growths especially, the hemorrhage takes place as the result of pressure necrosis or the active breaking-down process due to rapid development.

Many cases of nasal hemorrhage have occurred which have been traced directly to some constitutional disturbance. When the bleeding is from an apparently healthy nose some internal organ is probably at fault, in which case it may be stated that the blood comes through the nose, but not from it. It is not unusual to find this condition in many of the acute infections, as measles, scarlet fever, diphtheria, whooping-cough, cerebrospinal meningitis, pneumonia, influenza, erysipelas, and small-pox, but it is especially noted in typhoid fever. In various cases of circulatory disturbance where the patient is beyond middle life, and there is an associated increase of blood-pressure, a passive congestion of the mucous membrane is invariably produced which predisposes to bleeding, especially from the vascular area in the anterior portion of the septum. Such cases are particularly noted in mitral and tricuspid stenosis, aortic insufficiency, disease of the coronary arteries, aneurism, cirrhosis of the liver, chronic interstitial nephritis, and arteriosclerosis, resulting in apoplexy or endarteritis obliterans.

> When epistaxis recurs in elderly individuals it is in most instances a symptom of contracted kidney or of arteriosclerosis, and should not be passed over lightly. The writer cites cases in which this warning epistaxis, treated by tamponing without regard to the underlying trouble, has occurred a few weeks before apoplexy. Hummel (Fortschritte der Med., Feb. 10, 1908).
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> Epistaxis in old age is due to one of the following conditions:—
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> *Arteriosclerosis;* it may be profuse and frequent, capable in either respect of causing death—happily most exceptionally—it occurs in sclerosis, preferably during cold weather, sudden changes of temperature, fits of coughing, and after severe or prolonged effort and hearty meals.
>
> *Bright's disease* causes epistaxis in three ways, by the arteriosclerosis set up, the hypertension accompanying it, and the autointoxication giving rise to it.

> *Different affections of the liver*—hepatic congestion, atrophic and hypertrophic cirrhosis, malignant or simple jaundice, cancer of the liver—bring about epistaxis by the sclerosis and by the dyscrasia often associated.
>
> *Malarial disease,* chiefly in the cachectic stage, and *diabetes,* in all its phases, obtain their tendency to bleeding from the nose, partly from the sclerosis which they set up and in part from the alteration caused in the blood.
>
> *Heart disease* has an influence upon the etiology of epistaxis. Aortic lesions act by means of the vascular changes and the hypertension; mitral and tricuspid affections produce it by the mechanism of stasis, which follows upon the earliest appearance of hyposystole.
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> *Cerebral congestion,* often the prelude to cerebral hemorrhage, shows itself, and can sometimes be estimated by the amount, more or less profuse, of the bleeding. A sudden stoppage of the hemorrhoidal function, for example, in arthritis, gives rise to attacks of "supplementary" epistaxis, such as by an analogous mechanism are also met with during the menopause.
>
> *Hemophilia,* relatively uncommon in old people, comprehends epistaxis among the changes of its dyscrasia.
>
> Lastly, apart from all causes general or, at all events, distant from the nasal fossa, place must be found for local causes, the chief of which in old age are *epithelioma, sarcoma, polypi, syphilitic ulcers,* and *varices* of the mucous membrane, sometimes amounting to the formation of capillary aneurisms. Ranzier (Traité des maladies des vieillards; Practitioner, June, 1910).

Diseases of the lungs, such as chronic bronchitis, emphysema, pleurisy with effusion, empyema, and tumors pressing on the lungs, may be predisposing factors. Hemophiliacs have long caused physicians much anxiety because of their tendency to bleed, often on the least provocation, and of the difficulty frequently encountered to readily check the hemorrhage. Purpura, scurvy, and the secondary anemias sometimes add much to the danger of the patient, and the discomfort of the medical attendant, by the easy manner in which hemorrhage takes place. Vicarious menstruation has manifested itself by the escape of blood from the nose at the time of the menstrual period.

Notwithstanding the fact that a vigorous effort is usually made to check bleeding from the nasal cavities, one must not lose sight of the fact that such a condition may really be nature's safety-valve, as in cases of arteriosclerosis with increased blood-pressure; or that it may be the warning signal of the existence of cerebral hemorrhage, embolism, or thrombosis.

That cases are sometimes greatly benefited by the free flow of blood from the nose was evident in the report of 12 cases of cerebrospinal meningitis reported by Hays (New York Medical Journal, September 24, 1910, p. 605). In 4 of these cases epistaxis occurred, followed by a drop in temperature and the ultimate recovery of the patients. Of the remaining 8 cases, 3 succumbed to the disease.

The various changes which take place in the tissues in tuberculosis and syphilis not infrequently manifest themselves in the structures of the nose, and may sometimes result in nasal hemorrhage. Few of the drugs have been held responsible as being offenders, but distinct evidence has been produced against phosphorus, chloralamide, quinine, and the salicylic compounds.

Age, sex, and environment seem to be more or less significant in cases of epistaxis. The common period for the more frequent occurrence of this condition is from about the second or third year to puberty. As a rule, the adult is singularly free, but the tendency for a recurrence may manifest itself again in old age. Altered atmospheric pressure, as in balloon ascensions, mountain climbing, and diving, or even the extremes of temperature, may have a decided influence.

In some cases no demonstrable cause can be determined, and these are classified as (3) *Idiopathic.*

Just why bleeding should take place under these various constitutional conditions may be due (1) to alterations in the constituents of the blood; (2) to some disease within the blood-vessel walls; (3) to some obstruction to the circulation causing a strain of the whole system, and the nose suffering first because the vessels are superficial and in places the veins are enlarged to cavernous sinuses; (4) to the fact that the blood may be a vicarious discharge, or may be caused by the lowered resistance of the tissues to various chemical and bacterial toxins, or to a pathological change within the mucosa as the result of a local infection, but caused by a general disease. There is a possibility that the toxins produced in diphtheria may act upon the terminal nerve-fibers within the blood-vessel walls, producing a paresis of the walls, localized engorgement, and consequent rupture of the nasal mucosa at the weakest spot. In some cases of infection, however, it seems evident that the hemorrhage is due to the diminished resistance of the patient on account of the toxemia.

DIAGNOSIS.—In the great majority of the cases the direct cause for the nasal hemorrhage can be readily determined, but occasionally a case is encountered in which the evidence is quite obscure. The various infections and constitutional diseases will invariably give their associated symptoms. In the cases of hemorrhage as the result of high arterial tension, (1) the bleeding starts rather suddenly; (2) is usually profuse, often lasting for hours and frequently recurring at intervals of a few days until the blood-pressure is lowered; (3) the local treatment is seldom efficacious, and the usual styptics, cauterants, and packing prove to be of little or no avail unless measures of a general nature are instituted to reduce the tension. With the reduction of the excessive arterial pressure the hemorrhage ceases. In plethoric persons the bleeding may be preceded by headache; or in those persons prone to repeated attacks it may be produced by simply blowing the nose, sneezing, or introduction of the finger; or it may be spontaneous, even during sleep.

TREATMENT.—In the treatment of epistaxis there are several factors to be considered. As a rule, in the great majority of cases simple methods are readily efficacious; but if bleeding persists in spite of their application, search must be made for some constitutional cause. For instance, in cases of arteriosclerosis the blood-vessel walls are thickened and frequently contain deposits of lime salts, making it impossible for the necessary collapse to take place. At the same time the continuous stream passing over the ruptured spot usually does so with such force as to prevent any appreciable coagulation taking place.

Various remedies have been used in nasal bleeding, with more or less success in certain cases. A preparation of **cocaine**, gr. v (0.3 Gm.); **adrenalin**, ♏xx (1.25 c.c.); aqua, f℥ss (15 c.c.)—sprayed into the nose—will invariably prove successful in the majority of the milder cases. However, one may resort to the insufflation of finely powdered **alum** or **tannic acid**, or the use of an 8 to 10 per cent. solution of the same drugs.

> Instances of very alarming epistaxis in which all ordinary methods of stopping the hemorrhage were tried without success, and the patient was reaching a dangerous condition when **adrenalin**, in a strong solution, was used with most happy results. There was no further bleeding either immediately or secondarily. J. P. Booth (Southern Calif. Pract., July, 1902).

Solutions of **zinc sulphate**, **lead acetate**, or **copper sulphate**, gr. xxx to f℥j (2 to 30 Gm.), may be applied by syringe or pledgets; while **collodium** or a 10 per cent. **gelatin** solution may be smeared over the bleeding surface with a soft swab. Occasionally it is necessary to apply to the bleeding spot a solution of **silver nitrate**, gr. lx to f℥j (4 to 30 Gm.); a crystal of **chromic acid** fused into a bead on the end of an applicator, or even the **actual cautery**; but in resorting to any of these cauterants, one must guard against the marked destruction of tissue that may occur, and must aim as much as possible toward regeneration. When the bleeding is so profuse as to make it impossible to locate the area from which it is coming, douching of the nose with **hydrogen peroxide**, followed by a solution of **boric acid**, and then **packing** will frequently give gratifying results. In using the peroxide, however, the possibility of infecting the accessory sinuses must be remembered. Benefit is sometimes derived from using a hot douche of **phenol**, fʒj to Oj (4 to 500 c.c.) at a temperature of 105° to 130° F. (40.5° to 54.4° C.). A solution of **alum**, ʒij to Oj (8 Gm. to 30 c.c.), may be substituted with satisfactory results.

If necessary to apply pressure to the bleeding surface, it can readily be done with cotton or gauze, with or without one of the astringent solutions. Various preparations have been suggested for the impregnation of the gauze. A paste made by adding powdered **tannin** to a 20 per cent. solution of **antipyrin** has been used. **Beck's bismuth paste** has recently been advocated. Powdered **potassium permanganate** and **vaselin** appear to have adherents, while ʒj of **iodoform** to f℥j of compound tincture of **benzoin** has been used to advantage. If the gauze packing is soaked in sterile liquid **albolene**, and the patient given the same preparation and a dropper, and instructed to make frequent applications while in the recumbent position, it encourages healing and makes possible the easy removal of the gauze in twenty-four to thirty-six hours. The nasal chambers have also been packed with gauze soaked in **carbolized gelatin** solution. **Bernay-Simpson tampons** have been found extremely useful, especially if the bleeding is situated in the anterior portion of the septum. Casselberry suggests the insertion into the nose of a well-lubricated, clubbed-end, **rubber finger-cot**, and filling it with a yard or more of a 1¼-inch gauze.

> A **tampon** is used by the writer, composed of compressed cotton modi-

fied from Simpson's tampon, three inches long by one-half inch wide by one-sixteenth thick, wrapped as in a cigarette with gutta-percha tissue, the free edge being gummed down by some sterile ointment except at the ends. These smooth-surfaced tampons are easily and usually painlessly removed; they are deemed safer and much better than trusting to local medicinal applications in cases of postoperative hemorrhage. Sterile water or salt solution should be dropped on the ends to cause the tampon to swell and fill the passage. Two can be used side by side in very wide fossa and they can readily be narrowed by clipping. M. D. Stevenson (Jour. Amer. Med. Assoc., June 4, 1910).

The inflated **Rose bag** may be used, but in severe cases it will not give sufficient pressure to check the hemorrhage. Boyd (Australasian Medical Gazette, January 20, 1910, p. 26) has used a 5- or 6- inch square of finely starched linen, and inserted it into the nose to the nasopharynx with a pair of forceps or a penholder, and filled it with cotton soaked in any styptic; even **vinegar** may be used to advantage. Porcher (New York Medical Journal, 1909, xc, p. 331) **clamps** both nostrils with a clothespin or a stiff, bent hairpin, in order to allow the clot to form.

The author has frequently had success with the following procedure, originally suggested by Naegli: The patient sits upright in a chair, and the operator, standing behind him, places the index fingers of both hands beneath the body of the lower jaw on each side, while the thumbs rest behind the angles. Gentle traction is then made upward upon the head, which is simultaneously extended backward as far as the patient can comfortably bear, thus putting the muscles of the neck on the stretch. An **artificial anemia** is thus set up in the vessels of the head and also in the smaller vessels of the nasal mucous membrane, causing the epistaxis to cease. The procedure should not be continued longer than from one to two minutes, or a partial or complete loss of consciousness may result. Ritschl (Münch. med. Woch., Oct. 22, 1912).

On rare occasions it is necessary to insert a **gauze plug** into the nasopharynx. This is best done by passing a rubber catheter through the bleeding nostril to the postnasal space, pulling it forward in the mouth with a pair of forceps, fastening a piece of tape of at least a foot or more in length, with a gauze plug tied in the middle, and pulling the catheter back through the nose, at the same time guiding the plug with the index finger as it enters the nasopharynx. The nasal tape is pulled taut and tied firmly to a plug at the anterior nares. The end of the tape emerging from the mouth, to be used in removing the plug, is fastened loosely to the ear.

Apoplexy may result from plugging in epistaxis. A number of cases reported in which this has been the result, especially in the aged. In one case plugging with perchloride of iron produced erysipelas with very grave symptoms. Nasal hemorrhage opening the vessels of the nasal mucous membrane lowers the threatened arterial hypertension, frequently relieving the vessels of the brain and conducing to the safety of the patient.

The treatment should not be begun by plugging the anterior and posterior orifices. In young persons with healthy arteries this might be permissible, but plugging the nasal fossa in aged persons is dangerous. Perchloride of iron should never be used. Simple methods should be tried first, as **pinching the nose, elevation of the arms, cold water, key down the back,** etc. Afterward small **plugs steeped** in a **solution of antipyrin** may be applied through the anterior nares, or the **nasal passages** may be **irrigated with hot water.** These methods will be sufficient to at least moderate the hemorrhage, if not to arrest it. It is better in any case that the vessels open in the Schneiderian membrane than in the brain.

Dry cupping in the lumbar region, purgatives, mustard footbaths, applications of **hot water to** the **abdomen** should all be resorted to before plugging. Landouzy (Medical Press, July 1, 1903).

If **tampons** are at all resorted to, their long retention within the nose should be avoided, to eliminate the possibility of infection of the accessory sinuses; and, when inserted, should always be preceded by insufflation of powdered **bismuth subnitrate,** to avoid decomposition of the secretions.

The use of **Bellocq's cannula** should be reserved as last resort, as the instrument is very likely to cause injury, with secondary inflammation. The ears must be very carefully watched, and with the first signs of reddening of the drum membrane the packing must be removed. Thus the writer has seen several cases of otitis media with mastoiditis, and also empyema of the antrum, after the use of Bellocq's cannula. O. Mayer (Münch. med. Woch., Nu. 43, 1909).

It is frequently questionable as to whether the internal administration of medicines is of any benefit. Hypodermic injections of **morphine** have been advocated, and seem to work to advantage in keeping the patient quiet, even if not exerting a hemostatic action. In case of bleeders, when the arterial pressure is low, large doses of **strychnine nitrate** sometimes appear highly beneficial. Resort may also be had to the internal administration of powdered **opium,** gr. j (0.06 Gm.), with **lead acetate,** gr. ss (0.03 Gm.), repeated hourly for three doses, which shows a tendency to coagulate the blood. If the blood-pressure is normal, the administration of **adrenalin chloride,** gtt. v (0.3 c.c.) in water—every fifteen minutes—may work to advantage. Ten drops of a 1:2000 solution have been injected into the upper lip, on the side corresponding with the bleeding, and brilliant results have been reported. The internal administration of **gelatin** and the **calcium salts** is of doubtful benefit. Instances have been reported in which **serum** has proven beneficial, even **diphtheria antitoxin** being resorted to in an emergency. **Atropine** hypodermically is also effective.

In recurrent epistaxis the cause should be sought. The diet should be supervised, constipation corrected and all forcible movements avoided. The best drug to use is **digitalis,** usually in form of the titrated infusion. As a rule 0.7 to 0.8 Gm. (11 to 12½ grains) of digitalis given during two or three days is all that is necessary. Among 84 cases treated in this way, a recurrence of the hemorrhage was seen in only 2, where there was a tendency to hemophilia. The author believes that this excellent effect of digitalis is not due to any specific action, but that the drug merely overcomes the venous stasis and distributes the blood better over the body. Focke (Therap. d. Gegenwart, Sept., 1910).

Besides the well-known position with **ice** upon the nape of the neck, he advises internally 40 Gm. (1⅓ ounces) of 10 per cent. **gelatin** (calf's foot), which also can be given intramuscularly; furthermore, internally, 1 tablespoonful in milk, to be given every half-hour of the following: **Calcium chloride,** 4 Gm. (1 dram); syrup of mint, 50 Gm. (1⅔ ounces); water, up to 250 Gm. (8 ounces). A

> hypodermic injection of a rather strong dose of **morphine** has often good effects. Instead of morphine, **sodium chloride** up to 20 or 30 Gm. (⅔ to 1 ounce) may also be given, and **sodium bromide** up to 15 or 20 Gm. (½ to ⅔ ounce). Kobrak (Med. Klinik, June 2, 1912).

In all cases the patient should receive supportive treatment and careful nursing until health and strength have been restored.

Rufus B. Scarlett,
Philadelphia.

EPITHELIOMA. See Cancer.

EPSOM SALTS. See Magnesium.

EQUINIA. See Glanders.

ERGOT.—Ergot is a blight, the sclerotium of a parasitic fungus (*Claviceps purpurea*) which attacks and finally supplants the grain in the common rye (the *Secale cereale*). It is popularly known as "spurred rye," or "cockspur." It presents itself in grains of a slightly curved, fusiform shape, which are brittle, yet moderately flexible. Externally, it has a purplish-black color with longitudinal furrows on each side. It should be moderately dried, and should not be exposed to a damp atmosphere. It has a disagreeable, fishy odor, and a somewhat bitter, acrid taste.

Ergot is a complex substance containing a number of active principles, the most important of which are: *ergotoxine,* an alkaloid which is both a vasoconstrictor and stimulant of the uterus; *parahydroxyphenylethylamine,* or *tyramine,* a feebly basic epinephrin-like, strongly vasoconstrictor substance; *betaiminazolylethylamine,* or *histamine* (*ergamine*), even in great dilution, a powerful contractor of the uterus; *isoamylamine,* also a vasoconstrictor, but occurring in too small a proportion in ergot to influence materially its action.

> Ergotoxine is a highly active alkaloid, having the properties of ergot most desired in medicine. It brings about a long-enduring contraction of the walls of the arterioles, and increases the movements of the uterus. Its action is feeble when given by the mouth, but it is more marked in subcutaneous injections, and much more so when given intravenously. The last-named method is recommended in cases where a rapid and certain action is desired, either in **shock** or in **post-partum hemorrhage.** W. H. Cronyn and V. E. Henderson (Jour. of Pharmacol. and Exper. Therap., Aug., 1909).

> Ergotoxine acts more rapidly than the fluidextract and it can be given hypodermically. Ergotinine, however, is inert and useless. J. Gordon Sharp (Proceed. Royal Soc. of Med., May, 1911).

Recent work by various investigators, particularly Barger and Dale, has recently elucidated the composition of ergot and shown that ecboline, sphacelmic acid, cornutine, sphacelotoxin, and other familiar active principles so-called were mixtures of the above and other principles in an impure form.

> Number of tests of fluidextracts of ergot obtained from representative manufacturers, with the result that only two out of eleven samples were found to be active. The writers point out the mistake of the general idea that fluidextract of ergot is a stable preparation; in point of fact it deteriorates very rapidly. Wood and Hofer (Univ. of Penna. Med. Bull., Feb., 1909).

> Most galenical preparations of ergot contain considerable amounts of the active principles, but do not show any great or marked action when given by the mouth. The doses usually recommended for these prepara-

tions are much too small. When injected intravenously a fall in blood-pressure always precedes the rise, except after the administration of ergotoxine. Quantitatively, the galenical preparations of ergot show great variations in pharmacological action. W. H. Cronyn and V. E. Henderson (Jour. of Pharmacol. and Exper. Therap., Aug., 1909).

Ergot and its alkaloids deteriorate rapidly on keeping, the fluidextract of ergot, for instance, losing on an average about 10 per cent. per month. This may be avoided, however, by keeping it in Mulford's ampoules.

The ergot on the market varies greatly in its active principle, *i.e.*, in its power to cause unstriped muscle stimulation. A perfectly prepared fluidextract rapidly and continuously loses its activity and becomes worthless. The crude drug also loses its activity on keeping. Therefore, all liquid preparations of ergot should be kept in small bottles, hermetically sealed, and even then the label should declare at what date it is manufactured, since, if a preparation is old, it is of but little value. Ordinary fluidextracts, even if not exposed to the air, will lose approximately 10 per cent. of their strength per month; hence the ordinary fluidextract on the market, bottles of which are frequently opened, lose their strength much more rapidly, and are really generally worthless. H. C. Wood, Jr., and C. A. Hofer (Arch. of Intern. Med., Oct., 1910).

PREPARATIONS AND DOSE.—*Ergota*, U. S. P. (ergot). Dose, gr. 30 (Gm. 2).

Extractum ergotæ, U. S. P. (extract of ergot), which is incompatible with astringents and metallic salts in solution. Dose, 4 gr. (0.25 Gm.).

Fluidextractum ergotæ, U. S. P. (fluidextract of ergot). Dose 30 minims (2 c.c.).

Vinum ergotæ, U. S. P. (wine of ergot). Dose, 2 fluidrams (8 c.c.).

Ergotine is a term applied to various unofficial preparations of ergot, but is generally taken to refer to a watery extract of the drug purified by precipitation of certain constituents with alcohol. Dose, 4 gr. (0.25 Gm.).

Various other purified preparations of ergot, such as *cornutol, ergone, aseptic ergot,* as well as the three chief active principles themselves (see above) are on the market. *Ernutine* is a mixture of these three principles.

Subcutaneously.—Bonjean's *ergotine* (Fr. Cod.) and Squibb's ergotine are especially prepared for hypodermic use, 5 parts being dissolved in 7 parts each of glycerin and water and then filtered, 3 to 12 grains (0.2 to 0.8 Gm.—representing 120 grains—8 Gm.—of crude ergot) of the ergotine being the proper dose.

Ammonia is said to be the best solvent for the active principles of ergot, 2 parts of the former to 1 of the later being used, and the dose being 60 minims (4 c.c.).

PHYSIOLOGICAL ACTION.—Applied locally to mucous membranes ergot acts as a somewhat irritating astringent and hemostatic. On the skin these effects are very slight if at all appreciable.

Taken internally by the mouth ergot is absorbed with fair promptness, its action becoming manifest in from fifteen to twenty minutes and lasting about one hour. *Intravenously,* a moderate dose produces a marked rise of the blood-pressure; but if the dose be large, the rise is preceded by a fall of short duration. Very large doses or too frequently repeated doses may thus lower the blood-pressure below normal.

The typical effects of the *intravenous* injection of ergot consist in a large and abrupt fall of blood-pressure, followed by a prompt recovery, and generally by a slight and short rise. The volume of the organs varies generally in the same direction as the blood-pressure. The changes in the latter are mainly cardiac. This is confirmed by myocardiograms from the intact and excised heart. Ergot causes first a lessening and then an increase of the excursions; both phenomena may occur while the ergot is being injected. The rate of the heart is but little altered. The effect of ergot must be exerted directly on the cardiac muscle. There is some oncometric evidence that ergot has a slight vasoconstrictor action, but this is inconstant and inconsiderable. There was no evidence of strong constriction or of a high rise of blood-pressure.

The preliminary fall of blood-pressure is absent if the ergot is given by intramuscular injection.

The action of ergot is independent of the dose, within wide limits. The relative predominance of the fall and rise differs somewhat in different ergot preparations; age, however, does not impair the efficiency of their action on the mammalian circulation. The effects are greatly diminished by lowering the blood-pressure, by any method. Shortly after the destruction of the spinal cord, however, ergot produces a relatively good rise of pressure.

Large doses of ergot depress the vagus center and the vasomotor endings. It is not acutely fatal, even in very large doses. Torald Sollman and E. D. Brown (Jour. Amer. Med. Assoc., July 22, 1905).

Circulation.—The general effect of therapeutic dose is to constrict the peripheral blood-vessels, mainly through a direct action upon them and slightly by stimulating the vasomotor center, and thus to cause a general rise of the blood-pressure. The heart is also stimulated by moderate doses, but depressed by large ones. Its rate is usually slowed through stimulation of the cardioinhibitory center and the amplitude of the beats increased. These effects do not always occur, however, if the crude drug is used, since the histamine and certain other substances contained in it—choline, for instance—which tend to dilate the blood-vessels, may counteract the vasoconstrictor effect of the main active principles.

Ergot possesses the power to produce gangrene of the extremities. This is well shown by its action on the comb and wattles of roosters. This was formerly attributed to spasm of the arterioles, but is now believed to be due to the formation of emboli which obstruct the circulation.

Uterus.—Ergot powerfully stimulates the uterus and produces contractions through a local action on the motor endings of the hypogastric nerves, and also partly through excitation of the spinal "parturient" center. While small doses accelerate and strengthen uterine contractions large doses prolong the latter, finally causing them to tetanic spasms of long duration. As the various active principles in ergot possess a so different action on the uterine vessels according as to whether the uterus is pregnant or not—parahydroxyphenylethylamine, for instance—causing contraction of the pregnant uterus and relaxation of the non-pregnant organ, the effect of a given preparation is apt to vary according to the relative quantity of each principle it happens to contain; but inasmuch as the pregnant uterus is caused to contract more or less by all the active principles, and the use of ergot in connection with this organ is mainly in parturition, this action alone need interest us.

Ergot acts in **labor** in the following manner: (*a*) It collects the small irregular and non-effective pains into larger effective contractions, so that the labor is sooner ended and the uterus saved work. (*b*) It improves the tone of the muscle-fibers, whereby the uterus gains an advantage in that its musculature is ready at once to respond to further contraction, and thus neither time nor energy is spent in bringing the fibers up to that point at which contraction begins. (*c*) By acting on the abdominal muscles and on the muscular system generally, the tissues as a whole are improved in tone. This helps the uterus in its struggles.

The foregoing may be called the immediate benefits, but there is often a more remote beneficial action. (*d*) The forcible contractions following the administration of ergot, by expelling uterine contents, such as afterbirth, membrane, or other foreign body, relieve the organ of its troubles and set it free to recover itself in the ordinary way of nature. J. Gordon Sharp (Proceed. Royal Soc. of Med. of London, May, 1911).

Muscular System.—Through a specific action upon all the involuntary muscular fibers, ergot tends to stimulate the myocardium, the gastric and intestinal muscular coat, the bladder, the pupil, and all other structures provided with this class of fibers. Ergot thus tends to favor cardiac contraction, gastric and intestinal peristalsis, micturition when due to cystic atony, etc., besides acting on the blood-vessels as stated under the appropriate head.

Ergot is a stimulant to all the unstriped muscle tissue of the body. As a part of this general action there is a stimulant effect on the arterial muscles and probably also on the heart. The action on the blood-vessels occurs after destruction of the vasomotor center and, therefore, must be the result of an effect on some portion of the peripheral vasomotor mechanism. The degree of elevation of blood-pressure affords an accurate criterion of the activity of ergot and is, in their opinion, the most available method for the biological assay of the drug. Wood and Hofer (Arch. of Intern. Med., Oct. 15, 1910).

Elimination.—The fate of the active principles of ergot in the body has not as yet been determined.

Ergot was found in the feces of several different persons and dogs by the writer after its administration by the mouth. The microscopic findings were positive even after a single dose of 1 Gm. (15 grains). This is important in certain cases from a medicolegal standpoint for determining ergot poisoning in bread. The findings were positive only during from twenty-four to thirty-six hours after the ergot had been ingested. Strasburger (Centralbl. f. Gynäk., Bd. xxx, Nu. 49, 1907).

POISONING BY ERGOT.—Acute ergot poisoning is very infrequent. Very large doses of ergot produce symptoms of gastrointestinal and cerebrospinal origin. When taken by mouth ergot produces a heat and dryness of the throat, thirst; gastric pain, with nausea or vomiting; intestinal colic and diarrhea, giddiness, headache, restlessness and even delirium, coldness of the surface of the body, dilatation of the pupils, and a great retardation and slight weakness of the pulse.

Children and pregnant women are the first affected when rye bread containing ergot is eaten, sometimes only after several days.

Death may occur from cardiac paralysis.

The writer witnessed the following typical case of ergot poisoning: Early one morning he was summoned to a woman who was in a comatose condition. The pulse was 58, small, weak; respiration was labored; temperature 98° F. (36.7° C.). It was noted that the flexor muscles of the forearm underwent severe tonic contractions at intervals of a few minutes. Later the flexor muscles of the thigh and legs showed the same appearance. The toxic condition came on a short time before the patient was seen, and was initiated by giddiness and convulsions. The fluidextract of ergot had been taken in dram (4 Gm.) doses every four hours for four days before the symptoms developed. The patient was removed to the hospital, where she remained unconscious for three days. Constipation was marked, but urination was free. The pupils were widely dilated. Purpuric spots appeared on the neck, arms, and limbs. The pulse at one time was as low as 56, and for two weeks never went above 70. The patient ultimately recovered. F. M. O. Gorman (Phila. Med. Jour., Oct. 13, 1900).

Case of a man who had difficulty in breathing in the morning. The pupils were dilated, and the power of accommodation almost completely lost. It was then found that he had been taking extract of ergot. The patient was, therefore, given a vigorous diet, the ergot stopped, and he soon recovered. Schneider (Münch. med. Woch., Sept. 30, 1902).

Chronic ergot poisoning or **ergotism**, was formerly rather common, occurring in epidemics as a result of eating rye bread containing ergot. As the poorer classes of Spain and Russia relied mainly upon rye bread for their food, it was among them that ergotism was most frequently met. Two types of chronic ergot poisoning are encountered, the gangrenous and the convulsive.

Gangrenous ergotism usually affects the peripheral structures such as the fingers, toes, nose, ears, and sometimes an entire hand or foot, leg or arm, the genitalia, and also various internal organs. Cutaneous phenomena—tingling, formication, redness, coldness, an earthy hue, an eruption of vesicles containing a dark, ichorous fluid, and dry gangrene—follow one another in more or less rapid succession, muscular contractions complicating in a large proportion of cases. Nausea, vomiting, diarrhea, and colic are also observed.

Convulsive ergotism manifests itself mainly by disturbances of sensation, headache, a hard and small pulse, painful muscular cramps, and even by epileptiform convulsions, which are followed by marked nervous depression. These salient symptoms may be preceded by vertigo, tinnitus aurium, headache, itching, burning, and crawling sensations in the skin. Mental phenomena are common, the patient becoming somnolent, stupid, irresponsive and apathetic. Mania, melancholia, and other forms of insanity may be simulated.

> In 17 cases of psychoses from ergot poisoning witnessed by the writer, there did not seem to be any characteristic somatic feature of the ergot psychoses. The knee-jerk was variable, as also the sensory phenomena; exaggerated muscular excitability was more constant. The milder psychoses were not accompanied by any physical symptoms and in the severer cases the syndrome resembled actual tabes. The main cerebral features of the ergot psychoses were disturbances in consciousness and the emotional sphere, with more or less intellectual weakness and apathy. M. J. Gurewitsch (St. Petersberg med. Woch., Bd. xxxvi, S. 434, 1911).

Muscular tremors and contractures, especially of the flexors of the fingers and toes and of the extensors of the arms and thighs, are common. The majority of the symptoms of tabes may be present along with marked lassitude and emaciation. The organs of special sense are blunted, and the pupils dilated, though sometimes unequally.

Treatment of Ergot Poisoning.—In *acute poisoning* the bowels should be opened by quick purgatives: by **castor oil** or **Epsom salts.** **Tannic** or **gallic acid** should be given internally. The **recumbent posture** should be maintained, the patient be stimulated with **brandy** or other spirits, and given **amyl nitrite** by inhalation.

In *chronic ergotism* the treatment is chiefly hygienic and symptomatic on lines similar to those that apply to the acute form. In the gangrenous form the treatment is operative, it being advisable to wait for a line of demarcation and then to **amputate** immediately above the line. **Saline solution** intravenously should be tried, however, before operative procedures are resorted to if as soon as the cutaneous phenomena suggesting the possibility of oncoming gangrene appear. **Hypodermoclysis** is indicated in all cases as soon as the diagnosis of ergot intoxication is made.

THERAPEUTICS.—Ergot is mainly used by obstetricians and gynecologists to cause uterine contraction. Its use as an oxytocic is sanctioned by very few authorities.

Labor.—Full doses of ergot are never to be given to hasten the delivery of a fetus, because it causes tonic contraction of the uterus, interruption of the placental circulation, endangering the child through asphyxia, and if operative procedures be necessary they are greatly embarrassed by the rigidity of the uterus, and the danger of the uterine rupture is increased. There is a possible exception to this restriction. It may be given as a prophylactic against postpartum hemorrhage during the second stage of labor in those cases in which it is indicated, but not if there is any mechanical obstacle to delivery, or if the fetal head is high up in the canal. If it is given during this stage of labor the fetal heart should be carefully watched, and instrumental delivery resorted to if any signs of asphyxia occur. If ergot is given before the membranes have ruptured, it may prevent further dilatation of the uterus and deprive the fetus of its blood-supply. The drug may produce its effect prematurely if given at the time of passage of the child's head, and thus interfere with the expulsion of the placenta by producing hour-glass contraction.

> Instance of severe complications on account of the administration of ergot before the placenta had been expelled. The writer found 7 similar cases in German literature. In his own case delivery had been normal; two hours later the cervix permitted passage of two fingers and there had been considerable hemorrhage, but no signs of severe anemia, no dizziness nor fainting. As there seemed to be no change in these conditions, in a few hours the attending physician gave ergot and sent the patient to the hospital, where the cervix was found nearly closed. By this time fifty-five hours had elapsed since delivery of the child and there was a slight rise in temperature. After introduction of the inflatable bag for a few hours the placenta was evacuated by hand. Recovery promptly ensued. Schmid (Münch. med. Woch., Sept. 19, 1911).

The uses of ergot in parturition may be summarized as follows: (1) during labor, immediately after the birth, to keep the uterus firmly contracted and prevent post-partum hemorrhage; (2) earlier in labor, in occasional cases, to overcome dangerous inertia; (3) in subinvolution of the uterus.

It is especially indicated if an anesthetic has been required to effect delivery. It is useful as a prophylactic against, and a remedy for, post-partum hemorrhage.

The fluidextract administered by the mouth is generally preferred. When rapid effects are necessary, ergot may be given intramuscularly in preference to the subcutaneous method, which gives rise to considerable pain. A good preparation of ergotin in 10-minim (0.6 c.c.) doses may be employed for the purpose. Several new preparations, *ernutin, ergone,* and *aseptic ergot,* are particularly adapted to hypodermic use.

> To obtain the greatest therapeutic value of ergot in **labor,** it should be limited to, or near, the end of the third stage, administered by the mouth when indicated for the prevention of hemorrhage, and hypodermically when indicated for the control of hemorrhage. Applegate (Amer. Med., June 24, 1905).

Abortion.—Ergot is useful in this condition when the uterus remains relaxed, but is contraindicated before the uterus has been emptied. It is also useful in the subinvolution consequent upon abortions, given continually in small doses.

Nervous Disorders.—Ergot has also been found useful in certain mental diseases, as **epileptic mania** when associated with cerebral hyperemia, and **chronic mania** with lucid intervals. When given in large doses in **acute myelitis,** and in **congestion of the spinal cord and meninges,** it is said to be of value. Merits have been claimed for it in the treatment of **delirium tremens,** in conjunction with the bromides.

> In posthemorrhagic shock ergot must not be used, reliance being placed on increasing the fluid in the blood-vessels by transfusions of normal, sterilized salt solutions, and stimulating the heart by strychnine and alcohol. In uterine inertia, during the second stage of labor, it is wise not to give ergot, but to secure a sound sleep for the patient, to empty the bladder and rectum, and to apply forceps early, so as to lessen the risk of hemorrhage. Hooper (Intercol. Med. Jour. of Austral., Feb. 20, 1904).

> There is but one real indication for the multiple uses of ergot, which is the contraction of weak and relaxed unstriated fiber or other vital contractile tissue. By applying it ergot will be found a useful remedy in a large variety of cases, medical as well as surgical. Among these are affections of the heart, blood-vessels, and atony of the hollow viscera. It may be used to promote elimination and assimilation, to increase impaired functional activity, to regulate the menstrual functions, to counteract **insomnia, shock, neurasthenia, spasmodic nervous conditions, paralysis, coma, pain, toxemias, acne rosacea, varicose veins,** nervousness with defective venous circulation associated with **excessive cigarette smoking,** and surgical conditions. Alfred Livingston (Med. Rec., Nov. 23, 1907).

Hemorrhage.—In internal hemorrhage of various internal organs, especially in hemoptysis, ergot has been used because it contracts the blood-vessels in the bleeding area and tends to favor clotting. Inasmuch, however, as vasoconstriction occurs in all parts of the body, a general rise of the blood-pressure is produced which tends to counteract what hemostatic action it might have through its effect on the bleeding vessels. Its use therefore is no longer advocated in hemoptysis nor in cerebral hemorrhage, *i.e.*, apoplexy. In **renal** and **subcutaneous hemorrhages**, however, ergot has proven its value experimentally and clinically. Hence the fact that it is effective in **pulmonary edema** (but usually given with atropine) in **epistaxis, hematuria** (renal or vesical), **purpura hemorrhagica,** the **hemorrhage of scurvy,** etc. It has been used also in the intestinal **hemorrhage of typhoid fever,** in **dysentery** with bloody stools, in **serous diarrhea,** and in **bleeding hemorrhoids.**

Ergot may possibly effect a cure in small **aneurisms** of peripheral main arterial trunks by the contractions produced as the result of its action on the unstriped muscular fibers in the affected portion of the vessel. It also promotes coagulation of the blood in an aneurismal sac.

Diabetes.—Hypodermic injections are sometimes of value in **diabetes mellitus** to reduce the excessive flow of urine by causing vasoconstriction. The use of ergot combined with the bromide of sodium has been advised by Hare in the treatment of **diabetes insipidus.**

Genital Disorders.—Ergot has been employed with good effect in **spermatorrhea** and in deficient tone of the genital organs.

Locally ergotin is of value in **conjunctivitis,** incipient **boils,** and may be used in suppositories in such conditions as **prolapsed rectum** and **hemorrhoids.**

Clemins has used injections of ergot (4 grains to the ounce) into the bladder in the **cystitis** of paraplegic patients. The fluidextract may be employed as a local application in **chronic follicular tonsillitis,** and the oil is said to be of value in the treatment of **seborrhea.**

Ergot is used in **enlarged prostate** with retention of urine and in **enuresis.** Hypodermic injections about the dorsal vein of the penis are useful in **impotence** when relaxation of the organ occurs too early as a result of the too prompt return of the excess of venous blood to the general circulation.

C. E. de M. Sajous
and
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Philadelphia.

ERIGERON, OR FLEABANE.

—Oil of erigeron is a volatile oil obtained from the fresh, flowering herb of *Erigeron canadensis* Linné. It is of a pale-yellow color, having a peculiar, persistent, aromatic odor, and a slightly pungent, aromatic taste. As the result of age or exposure to the air it becomes darker and thicker. The specific gravity ranges from 0.845 to 0.865.

PREPARATIONS AND DOSE.—*Oleum erigerontis,* U. S. P., (oil of erigeron) is given in the dose of 15 minims (1 c.c.). It is best given in capsules. It is soluble in an equal volume of alcohol.

PHYSIOLOGICAL ACTION.—Oil of erigeron is an astringent and an active diuretic, being similar in action to turpentine, but less irritating. It is non-irritating to the stomach, and is said to have a slight tonic action.

THERAPEUTICS.—Externally, oil of erigeron may be applied to prevent **insects** from stinging, biting, or otherwise injuring the skin. Owing to its astringent action, oil of erigeron may be given internally for **hemorrhages** of a moderate degree. It is of most value in the treatment of passive **uterine hemorrhages** or oozing, and is also useful in **epistaxis.** In combination with cubebs and copaiba, it has also been used in the later stages of **gonorrhea.** In the treatment of **dysuria,** especially when occurring in children, the use of this drug will be found of value. It may also be used in **diarrhea, dropsical affections,** and in chronic forms of renal disease, its use being contraindicated in acute congestions of the kidney. H.

ERYSIPELAS.—DEFINITION.—By erysipelas is meant a violent inflammation of the superficial lymph-channels.

SYMPTOMS.—Erysipelas is most frequently found about the face and head, probably because of the excessive number of superficial lymphatic vessels. The affection has gradually lessened through the use of antiseptic principles in surgical practice.

It may occur in or extend to the fauces and tongue and, extending painlessly up the Eustachian tube, involve one or both eyes and may cause blindness (Snell). It has been observed, in fact, in all parts of the body.

> Erysipelas is far from rare in old people, although this is generally taught in the classical textbooks. If statistics give a small number of cases in old men it is because the disease is often benign and is unrecognized. According to Grisolle, erysipelas in old men becomes localized in preference in the lower limbs. In fact, the many other skin lesions which may be found so often upon the legs of old men, such as eczema, etc., may be the starting point for the erysipelas infection. The skin of old men becomes easily penetrable by the streptococcus, and the itching to which the skin lesions give rise, as well as the frequent slovenliness of old men, are contributing causes which also explain the frequency of the infection. Lucien and Parisot (Semaine méd., Dec. 11, 1907).

True cutaneous erysipelas is characterized by severe elevation of temperature, attended by a disseminated inflammation of the skin. This is sometimes preceded by a chill. The elevation of temperature continues until the erysipelatous process reaches its end. There may be a wound from which the redness starts, or there may be no cutaneous evidence of the seat of infection. A mere scratch, though healed, may have allowed the streptococcus to enter; having travelled up the lymphatics, the organism starts the erysipelatous process at a distance from the seat of entrance.

> Case in which a judgment for $5000 accident insurance was granted on the plea of accident, the death of the insured having been caused by erysipelas due to a slight injury on his cheek, causing a slight abrasion of the skin, which resulted in traumatic erysipelas. The attending physician testified to the discovery of the abrasion of the skin, and that in his opinion the disease from which the assured had died was wholly infectious, and could not have resulted except through infection of some wound or abrasion of the skin; that it made its first appearance at the edges of the alleged wound, and that in his opinion it resulted solely from the infection of that wound. (Jour. Amer. Med. Assoc., Sept. 21, 1912).

There may be red streaks showing lymphatic glands extending from the wound to the special place where the poison now develops very freely.

In the newborn, according to Lemaire, erysipelas may develop not only about the umbilical wound, but also around a vaccination wound and around the conjunctiva. Histological examination shows accumulations of streptococci in the lymphatic vessels. There may be a few bacilli in the superficial region of the derma, but none in the epidermis. At first the fever is not excessive, and it may not be noteworthy until the second or third day. If the child does not quickly die there may be several resulting abscesses, and death may ensue from the fifteenth to the twentieth day. If recovery follows it may be long in coming, being delayed by athrepsia or infectious diarrhea.

> Erysipelas in the newborn infant is a very serious and generally fatal disease. Its fatality depends on the absence of reaction against the germs, due to the absence of phagocytosis in the newborn child. After the age of 3 months the prognosis is quite otherwise because here phagocytosis goes on normally. Starting from the solution of continuity at the umbilicus the germs enter the tissues and are not opposed by the lymphatic glands. They enter the lymphatics of the subcutaneous tissues, where they are found in great numbers, as also in the outer coats of the blood-vessels. A rapidly fatal peritonitis closes the scene. The external redness and swelling are slight, the symptoms of peritonitis being the first sign. A. Herrgott (Annales de gynécol. et d'obstet., May, 1908).

Tension of the cellular tissues now becomes very marked; blebs may form on the surface from the intense irritation of the papillary layer of the skin. It sometimes happens that the process, having started in one part of the body, may be arrested, only to manifest itself elsewhere. As a rule, after the process subsides the parts are soon restored to their normal condition, although a certain amount of desquamation takes place.

When the deeper lymphatics are affected a great deal of effusion takes place in the cellular tissue, and cellulitis results, which is much more intense than that described as arising from the streptococcus in its ordinary degree of virulence. It bears, however, a great analogy to it, only the symptoms may be much more intense. A suppurative process takes place with a great disintegration of cellular tissue. This has been characterized as phlegmonous, or suppurative, erysipelas. It may come to the surface, and subsequently change its course as an erysipelas of the skin. It is also possible that other bacteria should contaminate this infection.

The constitutional symptoms correspond to the intensity and extent of the local process. The temperature rises to about 104° F., and may reach 107° F. The fever may be of a continuous remittent or intermittent type, and is in direct proportion to the extent of the inflammation. In some instances there occurs no fever, a probable sign that the immunizing functions are inadequate.

> Two cases in which the temperature was for the most part subnormal, although in both the cerebral symptoms were early and profound. This was perhaps due to the fact that there was very little effort on the part of either patient to combat the disease—the one being an elderly man of enfeebled constitution, and the other an infant 3 weeks old. Macauley (Brit. Med. Jour., Feb. 26, 1910).
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> The writer observed 29 afebrile cases, all in women, among his 324 cases of erysipelas in one year. Czyhlarz (Berl. klin. Woch., Sept. 11, 1911).

Gastric symptoms may likewise occur, with loss of appetite, nausea, vomiting, excessive thirst, and a highly coated tongue. The urine is generally dark colored, and may contain albumin, blood, bile-pigment, and micrococci. The spleen is sometimes swelled, and there may be pain in the region of the kidneys. An infective pneumonia due to extension of the disease from the oral cavity or pharynx may likewise occur. The heart is also involved in a large proportion of cases.

Erysipelas influences the myocardium. In about 500 patients with erysipelas examined, the writer found myocardial changes in about 250, dilatation of the heart in 44 patients. The changes pass away with the erysipelas without apparently leaving permanent injuries. The only physical sign seems to be the change in the outline of the heart. Teissier (Semaine méd., Jan. 12, 1910).

Two hundred and eighty-eight out of 2664 cases of erysipelas in the writer's service at Vienna were in persons over 60, that is, in 10.8 per cent. Only 91 of his elderly patients were men. He has been making a special study of the affection in the aged. Complications on the part of the respiratory organs were no more common than after other infections, but kidney affections were repeatedly encountered with erysipelas in the elderly, especially an acute hemorrhagic process subsiding with the infection. Nervous symptoms were frequent, sometimes mental confusion or delirium, even with an afebrile course of the erysipelas; occasionally there were ideas of persecution, but meningitis was scarcely ever observed in the elderly. The erysipelas attacked the face almost invariably; none of the patients presented erysipelas of a mucous membrane, although he knows of 1 case on record in which the throat was primarily invaded. Unusually frequent were the complications or sequels in the form of suppurative processes in the subcutaneous cellular tissue, especially when the erysipelas was on the limbs. There lesions ranged from abscesses and phlegmons to suppurative venous thrombosis and gangrenous processes. Gangrene of the lids was observed in a few cases, but the eyeball did not suppurate in any instance, and he witnessed the healing in some cases of a deep, extensive gangrenous process, even in women over 80. In 25 per cent. of his 288 cases of erysipelas in the elderly, it terminated fatally, but only 2 succumbed of the 15 patients who were over 80. H. Schlesinger (Med. Klinik, Aug 8, 1909).

Case of a healthy girl of 16, tending a woman with a severe erysipelas of the face, who was suddenly taken with serious peritonitis and succumbed on the fifth day. The autopsy revealed an acute streptococcic seropurulent peritonitis, but no sign of perforation; the genital organs were normal. This and several other cases reported by the writer indicate that erysipelas may be contagious during the prodromal stage, and that it may induce an isolated peritonitis, and that both the erysipelas and the peritonitis may have been drawn from the same source. M. Vallas (Lyon méd., Oct. 9, 1910).

If the process be not arrested, death may result from the extension of the local infection to some vital organ, as the brain or peritoneum.

In pregnant women, erysipelas, in the majority of cases, does not cause abortion. If confinement or miscarriage occur during its course, there is no genital infection, provided obstetrical antisepsis be rigorously practised; moreover, the children at birth, according to Le Gendre, show no trace of erysipelas.

Synovitis or suppurative arthritis may occur as a complication of erysipelas. In 817 cases of erysipelas recorded by Gamgee one or the other of these conditions took place. The complication may arise at any time during the attack. The suppurative form requires the promptest and most heroic treatment. Disorganization of the joint will follow, even the death of the patient, otherwise. Furuncles may follow an attack of erysipelas.

In a single case, Zeller and Arnold observed, in the course of a year and a quarter, about 650 furuncles, affecting all parts of the body, including the hairy scalp. Fever, up to 100° F.

and more, but without distinct relation to the abscess formation, was observed. There was little depression of the general health, and the termination was complete cure.

The kidneys, according to Pollatscheck, are affected in about 38 per cent. of all cases. This is evidenced in the kidneys by the presence of casts with or without albumin, of albumin with or without casts, or of both. The presence of even large quantities of albumin with renal elements in the sediment may be only transitory, and does not necessarily imply an unfavorable prognosis.

> Renal complications are to be expected with erysipelas. Of 483 reports of cases examined, 327 (67.7 per cent.) had excreted pathological urine. The mortality, however, did not apparently indicate that it was a very serious complication. In 66 of the cases the erysipelas was limited in extent; in 486 it was extensive. The scalp was primarily involved in 12 cases, but of the 485 cases beginning in the face in only 7 did the disease extend beyond the hair margin, the scalp remaining unaffected. Glycosuria occurred in a certain percentage of the cases. Boston and Blackburn (Jour. Amer. Med. Assoc., Nov. 2, 1907).

Death may result from exhaustion consequent upon the febrile process and weakening of the organs by gradual infection.

The duration of the infection is very uncertain. It may seem to have disappeared, and subsequently starts up again. It may last a few hours, and continue for several weeks. Again, it may travel over the whole body and possibly attack the same locality several times. As a rule, it delineates its course within two or three weeks.

Examination of the blood, whether made during an attack or during the period of convalescence, as emphasized by Chantemesse, furnishes valuable information regarding the course of an attack of erysipelas. The curve of the number of leucocytes in a case of erysipelas follows very closely that of the temperature, but this leucocytosis does not show equally throughout the various blood elements. The polynucleated cells show an increase as soon as the malady is established, while at the same time the number of mononucleated cells diminishes, such diminution occurring chiefly in the lymphocytes. When recovery takes place it is signalized by a fall in the number of polynucleated cells. The eosinophile cells, which fell in number during the course of the illness, only appear again when the blood infection is altogether at an end.

> In at least one-third of cases of severe erysipelas the blood yields a pure culture of the streptococcus. Such a finding does not however, imply an unfavorable prognosis. Streptococcic septicemia in a small proportion of cases and pyemia almost always may become complicated with infectious endocarditis. This involves the left side of the heart, particularly the mitral valve, which becomes covered with small vegetations. It is often overlooked, since generally there are no physical signs, though there is always a possibility of multiple embolism. Abnormal sounds heard over the precordium in erysipelas are only in exceptional instances due to endocarditis. Lesné, Françon and Gérard (Presse méd., Sept. 14, 1912).

Some persons are subject to "habitual attacks" of erysipelas, generally about the face, and probably repeated infections from a chronic nasal catarrh. As well shown by the researches of Christian C. Holmes (1907) the pneumococcus and streptococcus are the two principal pathogenic bacteria which have their normal habitat in the nose and accessory sinuses. Hence the relatively frequent occurrence of facial erysipelas with a primary infection in these cavities. In most instances, according to Lavrand, spontaneous recurrent erysipelas of the face develops from the nasal fossæ through the lachrymal duct or the nostrils. The point of departure is either in the nasal fossæ or, more frequently, in the more or less hypertrophied adenoid tissue of the pharyngeal cavity.

Erysipelas has no appreciable influence on the duration and amount of the menstrual flow. On the contrary, according to Salvy, menstruation favors the development of erysipelas. Recurrences during the flow are due to the peculiar nervous state of the patient and to the persistence of colonies of streptococci in the skin and lymph-spaces, whose virulence has not been entirely destroyed.

Case which is of interest on account of the presence of a mastoiditis during an attack of erysipelas. An operation was urgently demanded. In spite of the fact that such an operation was done within the erysipelatous area, not the slightest disturbance in the way of any serious complication occurred. Wiener (Med. Rec., Oct. 22, 1910).

Erysipelas of the larynx is more common than is generally supposed, though the literature does not indicate that the condition has been frequently met with or studied to any great extent. Some difficulty is occasionally encountered in making a differential diagnosis, for, while the local phenomena are generally very different from some conditions of the throat, as tonsillitis, they cannot always be distinguished from those of simple inflammation; and where only redness of the throat exists, it may be necessary to await the skin manifestations before a positive diagnosis can be made. The presence of phlyctenulæ in the throat makes the diagnosis less difficult, but adds to the gravity of the case, which may terminate even in gangrene.

The writer presents short histories of 3 cases, which show the seriousness of the condition and the necessity for early and energetic treatment. One case with a negative previous history became insane a few weeks after being discharged from the hospital cured, the mental derangement undoubtedly being due to the severe infection. D. Bryson Delavan (Laryngoscope, Mar., 1911).

Certain attacks of erysipelas have proved a source of immunity against anthrax, at least for a few days. There is a growing opinion that it exercises a direct effect against the development of sarcoma. Indeed, cases are reported of sarcomatous growths having gradually disappeared after an attack of purulent erysipelas; hence the practice of inoculating erysipelas in those suffering with inoperable sarcoma. This procedure is not, however, without danger to the patient, for it is not always possible to limit the development of the disease; hence the patient should be made cognizant of the risk to be run by the inoculation of erysipelas for the destruction of sarcoma.

In about a thousand cases of erysipelas, in over one-fourth of the number the affection was not recognized. Pure erysipelas is a mild, serous, and not a suppurative or destructive process; the patients should be protected against infections from other forms liable to superpose suppuration and necrosis on the erysipelatous process. Phlegmons are particularly dangerous in this particular. Sorensen (Hospitalstidende, Jan. 13, 1913).

The diagnosis of ordinary erysipelas is very simple. Gradually increasing and spreading redness is characteristic, and it can only be mistaken for *erythema.* This latter infection, however, is not accompanied by fever, while erysipelas always is.

The following three signs are characteristic: 1. The sign of centrifugal maximum. The most marked lesions are always situated at a spot at some distance from the starting point on the periphery of the patch; so also are the swelling and pain on pressure. This sign is useful in distinguishing erysipelas from inflammatory troubles, dacryocystitis, dental abscess, parotiditis or mumps. 2. The ear sign. Owing to the close adherence of the dermis and perichondrium, and the absence of subcutaneous tissue in the ear, inflammatory processes stop short at the periphery, whereas erysipelas, being a dermatitis, spreads in the thickness of the skin itself, invading that of the ear as it does in any other part. 3. The pain sign. The erysipelatous patch is invariably exceedingly painful. The patient invariably makes a grimace and shrinks when it is pressed, whereas in acute eczema and ophthalmic zona the parts are not so tender on pressure. In dental abscess and dacryocystitis, however, the affections are both painful and tender, but in a different way. Milian (Progrès méd., No. 30, 1908).

COMPLICATIONS.—The wound may apparently not be interfered with in the healing process, while at the same time a deep cellulitis exists, and may finally end in suppuration. The open wound upon which erysipelas has developed will take a dry, gray, dirty, and glossy appearance, covered with a sort of croupous membrane, and will retain this appearance until the intensity of the infection has disappeared. On the mucous membrane a swelled condition takes place, which may also cover itself with a croupous membrane. There may be marked disturbances of the central nervous system as the result of a high fever. Delirium and stupor, accompanied by vomiting and convulsions, may follow. A collapsed condition of the system may take place after the disappearance of the symptoms. Hallucinations and certain motor disturbances may occur. As a rule, the lymphatic glands are not affected in superficial erysipelas, while they may suppurate in a deeper form of the infection. Internal complications known as metastatic inflammations may take place. These may be septic bronchitis, pneumonia, or meningitis, while peritonitis may follow erysipelas of the neighboring parts. The local sequelæ of erysipelas are a thickened condition of the cellular tissue due to the obstruction of the lymphatic vessels and an impaired condition of the vitality of the skin, predisposing the parts to eczematous ulcerations. Deep cicatrices may also form as a permanent result.

ETIOLOGY AND PATHOLOGY.—Erysipelas is a violent inflammation of the lymph-channels, caused by the streptococcus. Although it is now generally conceded that the infectious agent, as described by Fehleisen as the cause of erysipelas, is identical with the streptococcus of suppuration, the symptoms of erysipelas are sufficiently different to warrant a description of this infection as a form of affection separate from ordinary suppuration. It has been proved that the virulence of the streptococcus varies materially with the nature of the soil upon which it grows; that it will frequently acquire a greater virulence when the resistance of the subject is lessened, as in tuberculosis, diphtheria, scarlet fever, small-pox, typhoid fever, and influenza, and when the vitality of the body is materially reduced, as by overwork.

> In the so-called idiopathic cases it is probable that in most cases we should seek for the cause in the air-passages of the patient himself. The streptococcus and the pneumococcus are practically always present in the normal nose and neighboring cavities. An increased virulence of the micro-organism or diminished resistance of the patient may bring on an attack. In a large number of cases the facial erysipelas followed an operation within the nose or accessory sinuses. In most of these it is probable that the disease was due to an autoinfection. Holmes (Annals of Otol., Rhin., and Laryn., Sept., 1907).

Its virulence materially differs in various animal organisms, as it is by no means equal to the virulence of the same streptococcus in mice or rabbits. Erysipelas can be produced in rabbits by the injection of the ordinary streptococcus of suppuration, and by that means acquire a greater virulence, and, if not attenuated, would reproduce symptoms of erysipelas in an ordinary wound infected with it. From its etiology, therefore, erysipelas is a non-specific disease, but is due to a higher state of virulence which the streptococcus happens to possess at the time it enters the tissues, or which it can soon acquire when the tissues are suited to its development in a virulent shape. It has also been demonstrated that erysipelas cocci may enter the blood; but, as a rule, they are not found in this fluid

> Erysipelas is an acute inflammation of the epidermis due to the presence of one of the organisms of the streptococcus class, of which the *Streptococcus pyogenes* is the most frequent example. Cellulitis appears to be a strictly comparable inflammation of the cellular tissues, and when the inflammatory processes involve both the epidermis and the cellular tissues the condition of cellulocutaneous erysipelas results. Acute lymphangitis would seem to be a less virulent infection, due, as a rule, to organisms of the staphylococcus class, with a greater tendency to spread, as its name implies, by the lymphatic system. Erysipelas is not, in the true sense of the term, a specific disease, since it may be produced by a variety of organisms, and these organisms are capable of producing other diseases. Panton and Adams (Lancet, Oct. 9, 1909).

Cold is a recognized etiological factor of erysipelas owing doubtless to the weakened resistance of the skin to infection it entails. Hence the more frequent occurrence of the disease in cold weather and the influence of cold draughts in causing the disease.

> Season has long been recognized as a prominent predisposing factor in erysipelas, the greatest number of cases, as shown by the histories of 564 cases, occurring during cold weather, and this is, in a measure, explained through the fact that men are more likely to suffer abrasions of the skin during the winter months. During June, July, August, and September, when in this climate we have our greatest heat, cases of erysipelas are few and, in fact, the rule is that during these months the erysipelas wards are often without a single occupant. Season also exerts a decided influence on the mortality rate, the greater proportionate number of deaths occurring during November, December, January, and February, at which months, in this climate, we

have our extreme cold. When the months of March and April are unusually cold the death rate is increased. Boston and Blackburn (Jour. Amer. Med. Assoc., Nov. 2, 1907).

PROGNOSIS.—The prognosis of erysipelas is very uncertain. The mortality rate is somewhat above 10 per cent. Much will depend upon the rapidity and intensity of the course of the infection, and upon the organs which may be secondarily invaded by the poison, or possibly a complication by which a septicemia may exist. Young and otherwise healthy persons would offer a favorable prognosis, while those more depleted, and especially those recovering from a lingering disease, would offer less hope of recovery.

Age is of great clinical importance both as a predisposing and prognostic factor in erysipelas. In their series of 564 cases studied, the writers found all cases developing in children during the first year of life were followed by a fatal termination, while between the first and tenth years the disease was not fatal. At the other extreme of life the mortality rate in erysipelas is exceedingly high, 83 per cent. of cases terminating fatally in those after the age of 80, and 38 per cent. in those between the seventieth and eightieth years. The duration of the disease in fatal cases is shorter during early adult and middle life than it is in the aged or in infants. It has been difficult to explain satisfactorily why this condition exists, Possibly between the ages of 20 and 60 erysipelas is apt to represent a highly virulent type of infection, and complications develop early and are severe in character. In the senile the erysipelatous process is liable to be of a low grade of infection and to spread extensively. Of the 539 cases analyzed with reference to sex there were 342 males and 197 females, while of the 69 deaths 56 of them were males **and 15** females. Boston and Blackburn (Jour. Amer. Med. Assoc., Nov. 2, 1907).

TREATMENT.—**Local.**—The multiplicity of remedies advocated for the treatment of erysipelas is the best proof that no specific exists to arrest this infection.

Comparative results of various treatments employed in 71 cases of erysipelas. In 37 the writer used a combination of **camphor** and **chloral,** 1 part of the latter to 3 of the former, with good results. The patients all recovered, and, although the treatment did not appear to affect the course of the disease, the patients gained relief from the application. In 10 cases **ichthyol collodion** was used with equally good results. In 5 cases **application of cold water** yielded good results, while in 5 other cases no treatment at all was given, except a little **calomel** and dilute **hydrochloric acid;** and the patients recovered just as quickly as did the others mentioned. In 3 cases every kind of treatment was tried, including the use of antistreptococcic serum, without avail. The patients died. **Red light** was tried in 3 cases. In the writer's opinion the treatment of erysipelas is expectant and that there is no specific for this disease. Potter (Jour. Med. Soc. of N. J., June, 1907).

Absolute alcohol is one of the older remedies in which most confidence can be placed in cases in which the occlusive bandage can be applied with exactitude, as, for instance, in erysipelas of the extremities. It is more difficult to apply where the face is the part affected, but the writer was able by its use to bring to a standstill after twenty-four hours erysipelas of the face in an old woman 82 years of age. For erysipelas of the scalp absolute alcohol is especially useful. A. Hecht (Therap. Monats., Jan., 1907).

The **hot-air douche** used in 19 cases of erysipelas caused rapid recovery.

The jet of superheated air was applied to the spot for half an hour to an hour two or three times a day. Absorption is promoted to such an extent that there is generally a slight rise of temperature afterward. The lesions were usually on the face and neck; when other parts of the body were involved a hot-air box or chamber or a hot flat-iron was employed. Ritter (Münch. med. Woch., May 24, 1910).

An ointment composed of 1 part of **chlorinated lime** and 9 parts of **paraffin ointment** proved to be the best application in 15 cases treated, the temperature falling in two to three days, instead of in nine, as with other methods of treatment. Not a single patient presented any serious complication. The salve mentioned is also excellent for the treatment of frost-bite. Very rarely, a patient will show an idiosyncrasy: here only a 5 per cent. ointment should be prescribed and should be carefully kept away from all open surfaces. If it is desired to remove the effects of chlorine, **sodium thiosulphate** may be used. C. Binz (Berl. klin. Woch., Nov. 1, 1909).

The writer has treated 77 cases of erysipelas differently localized, all serious and all occurring in women, with intramuscular injections of a 10 per cent. solution of **sodium nucleinate,** employing doses of 1, 2, or 3 c.c. (15, 30, or 45 minims). The injections were repeated every second or third day, and they exerted a decided effect upon the febrile temperature, the same being lowered permanently after the first injection in half of the cases, while at the same time the general condition and pulse improved considerably. M. E. Blumenau (Vratch, No. 45, 1911).

In the Polyclinic of Rome, over 1000 cases of erysipelas were treated in two and one-half years. Of these 87 died, but in only 47 cases was erysipelas responsible. The mortality from erysipelas is about 8 per cent., and chiefly in aged or debilitated persons. The various well-known measures for the treatment seem to have been of little value. **Hot compresses of** physiological **salt solution,** frequently renewed, reduced the heat and pain as much as the remedies tried, but did not affect the progress of the affection. T. Pontano (Policlinico, Rome, No. 1, 1912).

It is doubtful whether the antiseptics used externally in erysipelas can penetrate into the lymph-spaces and destroy the micro-organisms associated with the disease. Their application probably does not do more than prevent mixed infection. Among the antiseptics which may be used is **ichthyol** in ointment or aqueous solution of 10 to 50 per cent. strength, either painted on or applied thickly spread on lint or gause, which should be changed frequently to prevent drying or sticking. Similarly, there may be applied gauze saturated with a solution of **phenol** (1 to 2 per cent.), **boric acid** (saturated solution), **picric acid** (1 per cent), **sodium salicylate** (5 per cent.), **resorcin** (2 to 5 per cent.), **mercury bichloride** (1:5000), **lead and opium wash, magnesium sulphate, alcohol,** or simply **cold water.** A bolder method is the injection of antiseptic solutions a little outside of the margin of the advancing inflammatory process, *e.g.,* a 2 per cent. solution of **phenol,** or solutions of the **bichloride** or **biniodide of mercury.** The writer's favorite procedure in combating severe cases, however, is the continuous application of **ice** to the inflamed area. The parts are enveloped as thoroughly as possible, and where an extremity is involved it is placed in a trough of cracked ice for several days. A. P. Biddle (N. Y. Med. Jour., from Jour. Mich. State Med. Soc., May, 1912).

The writer has used, in the treatment of erysipelas, a simple remedy which is as certain as and even more rapid in its abortive action on erysipelas than the salicylate of iron. The remedy is **buttermilk,** which he orders to be applied on soft rags—buttercloth is excellent for the purpose—which are kept constantly wet with the remedy. F. S. Arnold (Practitioner, May, 1913).

Prevention, therefore, should be sought for. The greatest adherence to aseptic principles and in the subsequent dressings of the case will insure the impossibility of the wound's developing erysipelas. Should, however, a contaminated wound present itself with the developing disease, antisepsis must intelligently be applied to the particular case as our sheet-anchor. The various remedies advocated by different authors rest upon this principle, each only claiming his antiseptic to have given the best results. This is probably the case, because the particular author has had most experience in that special method. Of all the antiseptics, that which is commonly believed to have the most germicidal power is **1:1000 aqueous solution of mercuric chloride**, slightly acidified. The antiseptic must come in close proximity to the invading micro-organisms, in order that it should exert its destructive power. Any method which will facilitate this will fulfill the indications. I, therefore, believe, with Kunert, that multiple scarifications and incisions should be performed when possible in order to facilitate the direct absorption of the antiseptic solution, while I also advocate, with Riedel and Classen, the scarification of the advancing margins of the erysipelas, so as to cut the development across before the micro-organisms have had access to them and fill these developments with an antiseptic solution, and so destroy them as they advance. The parts are kept thoroughly irrigated with the **cold solution**. If the patient should have some idiosyncrasy against mercuric chloride, a 3 to 5 per cent. solution of **carbolic acid** may be used with efficiency. In fact, all the antiseptics known today have been, in turn, advocated, and, possibly, may be used with benefit.

Increase of virulence often occurs when infection is locked up in the subcutaneous tissues. The writer carried out experiments made to find whether or not it was possible to alter the virulence of staphylococci and streptococci so as to explain the clinical phenomena. He found that by taking a virulent strain of streptococcus and incubating it in an acid medium, the streptococcus changed to an apparently typical staphylococcus, while the same strain incubated in an alkaline or neutral medium retained streptococcic appearance and virulence. Earlier he had discovered that the acidifying of a bichloride of mercury solution would take away its action of coagulating the blood, thus rendering it more useful as an antiseptic application.

Applying these facts to the treatment of erysipelas, he used **acid, ice-cold bichloride of mercury** solution locally in the treatment of this disease, making minute scarifications, especially for two or three inches beyond the infected area, so as to lie upon the lymphatic vessels. The venous capillary hemorrhage thus caused allows vast numbers of the infecting cocci to escape, and the ice-cold compress, kept wet with the solution and applied to the lymphatic vessels, helps to destroy those remaining. If the infection is deeper, involving the cellular tissue, an incision should be made over the infected area for thorough drainage and disinfection. If the nose or some delicate part of the face is involved the scarifications may be replaced by copious acupuncture. He has employed this method in a large number of cases, both in hospitals and private work, with unfailing success in checking from the first the starting infection, and he believes that by this local treatment, in conjunction with the constitutional tonic treatment with tincture of chloride of iron, all the indications will be met. E. Laplace (Jour. Amer. Med. Assoc., July 20, 1907).

For erysipelas of the face and scalp **ichthyol and vaselin,** equal parts, form an excellent local application, placing over this absorbent cotton.

Magnesium sulphate in the form of saturated solution in water applied with compresses, kept constantly wet with the solution, and covered with oiled silk, has been found beneficial in a large number of cases.

Of the various remedies recommended for the treatment of erysipelas of the face **ichthyol** proved to be the most useful of all, applied in a mixture with equal parts of traumaticine. This was swabbed over the affected part three or four times a day, and the application was continued for forty-eight hours after all local symptoms had died out. Ichthyol may be used in many other ways, often to greater advantage. It may be applied pure, diluted with half its volume of boiled water, freely bathing the parts every day or twice a day. As it dries it forms a thick scab, thus rendering the use of successive dressings unnecessary. When all active symptoms have subsided it may be applied in an ointment. In the case of severe inflammation with oozing and suppuration it is better, for the first twenty-four or forty-eight hours, to apply dressings moistened with a 1 in 10 or 1 in 20 solution, applying the pure ichthyol at a later stage. In an ointment it is not so active and should be only used in cases with little inflammation:—

℞ *Ichthyolis*	ʒss (2 Gm.).
Zinci oxidi,	
Adipis lanæ	āā ʒij (8 Gm.).
Paraffini mollis q. s. ad	℥j (30 Gm.).

Misce. Fiat unguentum.

This is an excellent application when inflammation has disappeared. It should be used while redness persists, or the following cream may be substituted:—

℞ *Amyli*	ʒj (4 Gm.).
Zinci oxidi	ʒij (8 Gm.).
Adipis lanæ,	
Paraffini mollis ..	āā ℥ij (60 Gm.).
Liq. hydrogeni peroxidi	℥ss (15 c.c.).

Misce. Fiat cremor.

Should any telangiectasis persist the following ointment will be found more effective:—

℞ *Sol. adrenalini chloridi* (1:1000)	ʒss (2 Gm.).
Zinci oxidi,	
Adipis lanæ	āā ʒij (8 Gm.).
Paraffini mollis q. s. ad	℥j (30 Gm.).

Misce. Fiat unguentum.

Castaigne and Fernet (Journal de méd. et chir. pratiques; Amer. Med., April, 1912).

A mixture of 1 part of **ichthyol** with 2 parts of **alcohol** gives prompt benefit when used locally. The preparation should be freely applied, after careful shaving of the hairy surfaces, until the involved areas and even the surrounding zone of healthy skin have acquired a dark-brown color. Dind (Revue méd. de la Suisse Romande, May, 1912).

The writer found that the application of **magnesium sulphate** solution was extremely beneficial. Pain and swelling abated, fever decreased, and extension of the disease was controlled in the majority of cases. Report of 72 cases of erysipelas treated by wet dressings of a saturated solution of magnesium sulphate in water as originally advocated by Lucker. He used it in 19 cases of erysipelas complicated with alcoholism, acute nephritis, myocarditis, pneumonia, etc., with but 3 deaths, and in 35 uncomplicated cases without a single death. This treatment has been applied by him and others to nearly 700 cases of various forms of inflammation with uniformly good results. Lucker claimed originally the following advantages for it: The patient promptly obtains relief from the distressing local symptoms. The temperature rapidly falls to normal, usually during the second twenty-four hours, thus eliminating possible complications from a more prolonged fever. There is no necessity for internal medication in uncomplicated cases, the only treatment being a milk diet until the temperature becomes normal. In the writer's own cases pain and swelling abated, fever decreased, and extension of the infection was controlled in all but 6 cases. Many of the cases were advanced and neglected, and consequently the results have not been so uniformly good as those reported by Lucker. In 6 cases the inflammatory process extended so rapidly that in spite of this treatment antistreptococcus serum was injected; only 1 of these cases recovered. Excluding the above and 7 moribund cases, there remained 59 cases, with 13 deaths and 46 recoveries, equivalent to about 22 per cent. as compared with about 16 per cent. in Lucker's complicated cases. Choksy (Lancet, Feb. 4, 1911).

Hueter has recommended the parenchymatous injection of 2 or 3 per cent. solution of **carbolic acid** at the margin of the inflamed district, particularly in the beginning of erysipelas.

The **carbolic acid** may also be painted over the erysipelatous area and to wash it off with **alcohol.**

The writer's routine treatment is to paint the area with pure **carbolic acid,** extending the painting about three-eighths of an inch beyond the line of demarcation. This is allowed to remain until it becomes white, when it is washed off with 95 per cent. **alcohol.** The penetrating action of carbolic acid is a direct germicide to the streptococci already present, and the ring around the area serves as a strong barrier beyond which it is almost impossible for the infection to spread. This line of treatment causes an intense smarting and burning which lasts but a few moments and is quickly relieved by alcohol. In some cases the burning continues for an hour or two in which a cloth saturated with alcohol is laid on the area. In case of extension into the eyelids, where it is impossible and impractical to use the pure carbolic acid, the writer prescribes a **2 per cent. carbolic acid solution in unguentum hydrargyri ammoniatum** to be applied frequently. In 12 cases of erysipelas so far treated in this manner, the results have been the same in every case. More than two applications are unnecessary, one application being usually sufficient. Allen (N. Y. Med. Jour., July 11, 1908).

The general condition may be gauged by the severity of the skin affection, its intensity and area; hence the writer directs his energies to controlling the local focus of infection. By these means he has a record of nearly 300 patients treated successfully from the onset. He has tried without success all the ordinary measures of local treatment and falls back on the following:—

℞ *Carbolic acid*	3 parts.
Spirits of camphor	6 parts.
Alcohol	1 part.

The amount of the acid is large; it readily penetrates the entire skin, destroys the infection promptly and leaves no scars, and causes no pain and but little smarting. The camphor prevents the burning effect of the phenol. A larger percentage of alcohol destroys the acid action too greatly. In mild cases one application a day is sufficient, extending fully an inch beyond the edge of infection. In more severe cases two or three applications a day may be made. It can be used often without fear of an untoward result. If the skin is very hot or dry the area may be covered with gauze wrung out of cold sterile salt solution. Davis (Med. Bulletin, May, 1909).

The writer reports 82 cases of erysipelas treated by means of **carbolic acid** and **alcohol** during the past eight years. There were 67 complete remissions of symptoms in from twelve hours to four days. There were 10 delayed recoveries, and the treatment failed in 5 of the cases. The technique of the method consists of painting with a swab of cotton the entire surface of the involved area, and extending about half an inch into the surrounding and apparently healthy skin, with a 95 per cent. solution of carbolic acid. This is left until the purplish color of the inflamed area is replaced by a pretty complete whitening of the skin. When large areas are involved, it is advisable that only a portion be painted at a time. The second step consists in going over the whitened areas very thoroughly with a second swab saturated with pure alcohol. The swabbing with the alcohol must be kept up until the whitened area becomes pink. Half an inch of the surrounding skin must be included, as the bacteria of erysipelas are found beyond the apparently involved area. This method includes the painting of the hairy scalp, the eyelids, the mucous membrane of the alæ of the nose, and the nipple of the breast, if necessary. The writer failed to note any bad results from this treatment. Judd (Med. Record, vol. vii, p. 268, 1909).

In cellulocutaneous erysipelas and cellulitis a series of **incisions**, each about two inches long, should be made in the inflamed cellulose tissue in order to prevent gangrene and give exit to the pus or discharges. These incisions are made where the skin seems to be most inflamed, in the direction of the long axis of the limb, parallel with the blood-vessels, so that these should not be wounded. It may be necessary to give an anesthetic to make these incisions.

General Treatment.—General treatment will essentially consist in feeding the patient and giving tonics; chief among these will be the tincture of the **chloride of iron** in doses of 30 drops every two hours. This is supposed to have more of a specific action than any other drug recommended for the purpose.

The best **diet** will be milk, beef-tea, eggs, champagne, and beer.

The **bowels** should be **regulated**, and an **anodyne** given to induce sleep and relieve restlessness.

A number of Italian and Russian observers have reported beneficial results from the use of **diphtheria antitoxin** in erysipelas.

Report of 7 cases of facial erysipelas treated with **diphtheria antitoxin** injected subcutaneously and applied locally. The effects were eminently favorable. The writer used 10,500 units, giving 1500 by injections and the rest by local application. The last patient was a man of 50, and other measures were suspended after this treatment was commenced. Federici (Gaz. degli Ospedali, Oct. 20, 1907).

Injections of **diphtheria antitoxin** seems to favor the production of these substances and thus to promote phagocytosis—its action re-enforced by its power to induce leucocytosis. The benefit from the antitoxin was marked in his 3 clinical cases, as also in a number that have been reported. Migliacci (Gaz. degli Ospedali, Sept. 16, 1909).

The writer witnessed a rapid fall of temperature with disappearance of the skin manifestations after the injection of ordinary **diphtheria antitoxin.** In a few cases, a second injection was necessary to bring about the desired effect, while in a smaller percentage, usually of far-advanced cases, the serum was ineffective. Sometimes the symptoms of the disease itself disappear, but septic complications develop later. In other streptococcus infections, the serum was useless, so that it is as yet impossible to explain its action in erysipelas. O. Polak (Wiener med. Woch., July 22, 1911).

Vaccine therapy has also an increasing number of advocates, but it is difficult at present to reach a final conclusion as to its actual value. (See also Bacterial Vaccines, in the second volume.)

Erysipelas has yielded so little to treatment in the past that it is not wholly strange that many medical men have abandoned therapeutic remedies, used supportive treatment and hoped for a living patient after the disease had "run its course"—*i.e.,* developed sufficient specific resistance in the body to check further spread of the disease. The writers employed **bacterial treatment** in 3 cases of erysipelas, injecting dead streptococci with apparently uniformly good results. The dose in these cases varied from 30,000,000 to 60,000,000 dead **streptococci.** Duncan and Illman (N. Y. Med. Jour., Sept. 19, 1909).

Series of 50 patients, the first 16 of whom were treated according to the opsonic principles of vaccine therapy, but these revealed such a uniformly satisfactory immunizing response and clinical result that the writers felt justified in attempting the administration of the **erysipelas vaccine** without the usual blood examinations. If they are right in their conclusions that erysipelas vaccine when properly administered is a specific remedy for erysipelas, then the importance of being able to omit the laborious opsonic investigations becomes exceedingly great, for it puts into the hand of every practitioner of medicine a new specific for an exceedingly troublesome affection for which as yet only a multitude of remedies of alleged efficacy is available. It is entirely unnecessary to prepare a vaccine for each case. It is, however, advisable to have a composite stock vaccine derived from several different strains, from as many different cases. It is probable that the more virulent the case of erysipelas the more valuable will its streptococcus be as a vaccine. The method of treatment has been, in almost every case, to inoculate with 10,000,000 of the devitalized streptococci on the first visit if the case is a severe one, and with 20,000,000 if it is less severe. On the second day in the severe case the patient gets 10,000,000 more if there are signs of improvement. The most important of these signs is a certain clearing of the intellect, and the others are a lessened intensity of the local condition—less tenderness and pain. The temperature is not so satisfactory a guide, although a fall of two or three degrees on the morning following the injection is a valuable indication for a second inoculation. Ross and Johnson (Jour. Amer. Med. Assoc., Mar. 6, 1909).

Vaccines, both autogenous and polyvalent, have a decided and important place in the treatment of erysipelas. The writer treated 30 cases with a stock vaccine prepared from several patients, and to which was usually added a number of strains of streptococci obtained from various other virulent infections. In addition, this treatment was supplemented by autogenous preparations whenever possible. The first dose was given as soon as the diagnosis was evident, and followed after one or two days by a second, third, or fourth. Five or ten million organisms were usually given at first; later, ten or fifteen million.

The vaccines seemed decidedly to abbreviate the course of the disease. In several cases where the prognosis had been very grave, their use was followed by convalescence. The vaccines also promised much in the prevention of recurrent attacks; 3 of the 30 patients treated died, but in these the condition had been so desperate that no results could be expected. In 3 cases in which there had been repeated recurrences up to the time of treatment, no further attacks occurred. W. H. Walters (Amer. Jour. of Dermat., July, 1912).

The use of **antistreptococcic serum** in the treatment is advocated by some observers and condemned by others. Its successful use, however, usually coincides with its early employment in a given case and with large doses. The effect of a successful serum injection is not manifested for twelve to twenty hours, and reaches its maximum in twenty-four hours. The morning temperature is therefore more apt to show the influence of the serum than the evening temperature, if the injection has been made the previous evening. The most noticeable effect is the reduction in temperature, which is accompanied by a more or less profuse perspiration. But before this, the influence on pulse and respiration is already marked, the patient becomes quieter and breathes easier.

> When introduced into the system of a patient suffering from a local or general streptococcus infection, the **serum** will almost always exert its bactericidal properties upon the germs. A large amount of intracellular toxin (endotoxin) is, however, set free as a result of the disintegration of the germs, and it may well happen that the body can no longer resist this sudden poisoning. It is for this reason that quite a number of cases have died more rapidly than they probably would have if not treated with serum. If the patient is still in good condition, as where the serum is used early in the disease, good effects are seen more often. In erysipelas, the process has usually advanced too far to be affected favorably by the serum when the latter is used. Menzer (Berl. klin. therap. Woch., Nu. 44, 1904).
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> The writer usually gives from 1¼ to 3½ drams (5 to 14 c.c.) as a daily dose, and administers a short time before each injection a saline infusion of about half a pint. Erysipelas is favorably affected by the **serum**, but the redness may increase following an injection. F. Meyer (Berl. klin. Woch., Nu. 8, S. 197, 1905).
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> Series of streptococcic cases showing that the **serum** will well justify its use in the results obtained, even though, from the many forms of streptococci known and our very frequent inability to determine the streptococci as the existing cause of any given case, its use may be to a great extent empirical, provided that it is used as soon as possible, in maximum doses, and in dosage frequently repeated. W. D. Roussel (N. O. Med. and Surg., Nov., 1908).
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> Proofs of the effectiveness of the **antistreptococcic serum** treatment are wanting in many cases of erysipelas, but this is due mainly to the inadequacy of the dosage. Instead of using the ordinary prescribed dosage of from 20 to 40 c.c. the patient, an extremely bad case, was given 200 c.c. injected into the muscles of the back and repeated in twelve hours, making 400 c.c. within twenty-four hours. There was a very decided improvement; at the expiration of twenty-four hours the delirium disappeared and the patient's temperature fell 3 degrees. All the symptoms began to recede rapidly and on the eighth day the temperature had reached normal. All symptoms had subsided on the eleventh day. M. A. Bahr (Indianapolis Med. Jour., July, 1912).

Ernest Laplace,
Philadelphia.

ERYTHEMA — **DEFINITION.**— Erythema in itself simply denotes redness of the skin in which varying graduations of tint from yellowish red to violaceous red, darkish red, bluish red, or even blackish red are observed. As a disturbance of the functions of the skin it implies, on the one hand, various forms of hyperemia or active inflammation.

SIMPLE ERYTHEMA.—In this form there is a discoloration of the skin, varying in tint, size, and shape, and due to an abnormal flux of blood to the tissues without the presence of inflammation.

Symptoms.—The affection is transient, the coloring fading under pressure, and is caused by numerous internal and external agencies. It is instanced by the abnormal flushings and blushings, which are the expression of the varied feelings, such as anger, joy, and shame; it is also produced by disturbances of digestion due to indigestible foods, alcohol, drugs, or by various external injuries, as, for instance, the action of heat or cold, poisonous plants or drugs, or traumatism. The lesions produced vary from the slighest tint of red to a very dark color, and vary in shape from a round or oval to an irregular patch.

Erythema Pudoris. — This form bears considerable analogy to the above, but it is the expression of menstrual disturbances, pregnancy, climatic influences, and general disorders. The difference between this and the foregoing variety lies in the cause. This latter affection is the result of some physical influence, and usually progresses as the patient ages. Chronic blushers belong to this category.

Erythema Venenatum.—Certain mineral and vegetable substances also produce an erythema, but if the contact is prolonged actual inflammation takes place, and vesicles, pustules, or other symptoms may be observed. This form of erythema occupies the point of contact, and is manifested by a distinct, pinkish-red, irregular patch of small or large size, according to the amount of surface acted upon by the irritant. Mustard, cantharides, sulphur, strong soaps, ivy and other plants, acids, and many other drugs may be mentioned as some of the causes. This form of erythema usually persists for some time after the removal of the causative influence, and in cases in which the skin is delicate the most energetic treatment will be demanded.

> Case of a man who acquired syphilis in March, 1904, later developed certain manifestations of syphilis on account of which he was put on mercurial treatment in February, 1905. A few days later a circinate erythema appeared on his left thigh. The mercury was discontinued and the eruption disappeared. In February, 1906, the patient was again given mercury with the result that three days later the eruption reappeared and continued to augment until the cessation of the administration of the mercury. The eruption belonged to the class named by Hebra multiform exudative erythema. Bonnet (Lyon méd., Sept. 16, 1906).

Erythema Caloricum.—Both heat and cold may give rise to erythema. That induced by heat is diffuse, and, although its disappearance follows immediately upon the withdrawal of the causal factor, it may persist for some time in fair skins, to be, in turn, followed by some degree of desquamation. Exposure to the actinic rays of the sun is the usual and greatest exciting cause, although it is observed in many persons who are obliged to work around stoves or machinery.

Cooks, stokers, and men or women who warm their limbs before the open grate present gyrate patterns and annular patches of redness (*Erythema ab igne,* Crocker). This condition generally disappears without leaving any trace, but there are cases in which the causative influence is often repeated; some degree of pigmentation is induced and may persist for long periods, if it is ever at all removed.

> Four cases of reticulate erythema and pigmentation due to long-continued exposure of the skin to heat; they were decidedly below the normal standard of health either as a result of previous illness, alcoholism, or old age. In 1 case the erythema occurred in the lower part of the back and was the result of the continued application of a hot-water bag. Sections of 1 of the cases showed pathological changes of an inflammatory type consisting of cellular infiltration in the papillary and subpapillary layers and in the vicinity of the vessels. All the sections showed a more or less marked deposit of brown pigment in the basal cells of the rete mucosum. The microscopic changes showed the affection to be clearly inflammatory and not simply a staining of the skin with blood-pigment as has been suggested. M. B. Hartzell (Jour. of Cutan. Dis., Aug., 1912).

Hammer refers to certain cases in which the action of the sun's rays disappear immediately upon entrance indoors, and speaks of these cases as not being influenced by the heat of a fire, but as being observed in winter as well as in summer. Cold exerts a similar influence upon certain subjects and is shown by a livid, bluish, or cyanotic appearance at the point of contact. Exposed for long periods pigmentation may be observed, or the condition may terminate in inflammation or ulceration.

Erythema Traumaticum.—Violence of slight degree causes a diffuse redness at the point of contact, which may vary from a slight tinge of yellowish red to that of a dark red. Even under slight traumatism, if contact is allowed to continue, the condition will induce inflammation with all its consequent phenomena of vesicles, pustules, or bullous lesions. Complications may arise in the form of a true dermatitis, eczema, or other form of irritation or ulceration, and permanent pigmentation follow.

The exciting agencies are numerous, and the degree of injury depends upon the actual cause. Ill-fitting wearing apparel or even bed-dressings, tight garters, shoes, trusses, and diapers are some of the factors most commonly met with, while feces and salivary and leucorrheal discharges may represent another class among causal conditions.

> There are at least four distinct types of eruptions involving the napkin region of infants, which are of non-syphilitic nature and which must be carefully distinguished from the eruptions of congenital syphilis. The most frequently occurring of these are the various forms of erythema of Jacquet: (1) Simple erythema is found oftenest on the prominent convex surfaces of the buttocks and neighboring parts; in severe cases it may extend to other parts of the body. It is most common in very young infants. (2) The erythematovesicular type presents in addition, toward the center of the convex area, small bright-red erosions; at the periphery of the erythematous areas are small vesicles; the erosions by coalescence denude large areas. (3) The erythematopapular type has flat, red papules on an erythematous base. (4) In the ulcerating form the erosions have gone deeper instead of granulating. The last three forms occur in infants several months old. These four forms depend upon a vasomotor disturbance, possibly of gastrointestinal toxic origin, with a determining factor of local mechanical irritation. The seborrheic dermatitis occurs in babies a few months old. The entire napkin region is involved. The eruption is bright red, small scales being over all. Other parts besides the napkin region are also involved, more particularly the scalp, umbilicus, behind the ear, etc. The cause of the condition is microbic and the cure a daily boric acid bath, with sulphur ointment (10 grains to the ounce). A third class of eruptions is the vacciniform ecthyma; it resembles the erosive and ulcerative stage of Jacquet's erythema, and is of streptococcic origin. The bullous impetigo is also streptococcic. It is usually found in other parts of the body besides the napkin region. The phlyctenular margins reveal the impetiginous nature of the bullæ denuded of their epidermis. H. G. Adamson (Brit. Jour. Dermat., vol. xxi, p. 37, 1909).

Repeated attacks leave the point of affection prone to other affections; the most important of these is bed-sore, which occurs as the result of being too long in one position and thus inducing pressure upon one portion of the body, or lying upon rough and unclean bed-linen. Certain occupations tend to the production of local erythema, as, for instance, in the case of persons who are obliged to remain seated for long periods, as shoemakers, or those who stand indefinitely, as clerks.

Erythema Neonatorum.—During the first week of life we sometimes meet with a diffuse universal redness; according to Elliot, this rarely extends beyond the seventh day. Beginning as a pale-red spot, it reaches its highest coloration about the third or fourth day, and then gradually fades, without leaving any desquamation. Elliot states that "during its involution, a yellow color, resembling that of icterus, may become apparent, and in very severe cases there may be petechia." The usual causal factor in its production is some form of external irritation, harsh manipulation, either with the hands or towel while bathing or dressing, and exposure to the atmosphere.

ERYTHEMA LÆVE.—This term is applied to red patches apparently produced by edematous conditions of the limbs; impaired circulation is the probable cause. Swelling, redness, tensity, and a glossy or waxy appearance of the skin are the usual symptoms met with. Allowed to continue, these symptoms usually terminate in ulceration. Erythema edematosum is applied when great edema is present.

ERYTHEMA SIMPLEX SYMPTOMATICUM.—Under this heading belong all the erythemas which are due to some internal derangement, whether of the intestinal canal or from some general disease of the system. In some instances the cause is the ingestion of some food which retards digestion; in others the general economy is disturbed by some drug, such as alcohol, phenacetin, or other substance. This form of erythema does not respect any portion of the body; it most frequently attacks the face, neck, and upper portion of the chest and back.

ERYTHEMA INFANTILIS.—Erythema in th infant results from derangements of diges tion, teething, and a number of other affections to which young children are prone. It appears, for the most part, upon the face and trunk, although other surfaces are liable to be affected. It may vary from a rosy-red macule of diminutive size to a lesion circular or semicircular in form, or present multiform manifestations. It is rarely elevated, causes some itching, but usually disappears in a few days. It may be persistent if its causes are not removed, and is sometimes followed by a slight desquamation.

> Case of a child under 2 years of age in whom death followed an erythematous eruption secondary to intestinal catarrh. Nuwin and Eddowes (Brit. Med. Jour., Feb. 3, 1912).

ERYTHEMA MEDICAMENTOSUM.—The lesions produced by drugs internally administered upon the skin are manifold in character and may at times resemble many other diseases of the skin, but the fact that one of a series of eruption-producing drugs—such as the coal-tar derivatives, antipyrin, antifebrin, phenacetin, and others—as salicylic acid, quinine, and iodine—has been ingested will generally lead to a correct solution of the difficulty. (See DERMATITIS and the various drugs named).

> Case of a man of 37 who had taken moderate doses of Fowler's solution for furunculosis during almost six weeks, when an eruption appeared on his hands, feet, thighs, and scrotum. Large bullæ formed upon an erythema, and crusts were noted upon the scrotum. Besides, there were marked constitutional symptoms, all of which gradually disappeared during the two weeks following the cessation of the arsenic. This is the first reported case of a bullous eruption due to arsenic. Neumann (Wiener klin. Woch., Nov. 21, 1901).
>
> Erythematous and urticarial rashes are usually of toxic origin, as witness their development in some individuals after taking certain articles of diet or drugs, or as the results of stings of insects or of nettles, or of contact with caterpillars of certain species. One must suppose, therefore, that the lesions of joints which accompany them are likewise due to toxic influences. Garrod (Lancet, May 27, 1911).

ANOMALOUS FORMS.—Under this heading may be included forms mentioned by Duhring as occurring in the course of asthma, rheumatism, gout, hemiplegia, chorea, epilepsy, exophthalmic goiter, and other toxic influences.

> Case of recurring erythema in a tuberculous woman who had five recurring attacks of an eruption resembling that of scarlet fever, succumbing in the last attack, which was of a hemorrhagic nature with femoral thrombosis and gangrene. Some of the attacks seemed to develop spontaneously, while others followed the administration of antipyrin, etc, and are evidently due to idiosyncrasy or anaphylaxis. The first attack was diagnosed as measles, the second and third as scarlet fever. Devic and Gardère (Revue de méd., April, 1911).

This variety also includes the form observed during variola. It may be noticed about the second day of small-pox, and before the appearance of the specific eruption. According to Atkinson, of Baltimore, it generally spares the portions usually invaded by small-pox and rarely lasts more than twenty-four hours. The character of erythema observed is a diffuse redness, of a violaceous color, and in size varies from a pinhead to a Lima bean.

> Measles is often confounded, both by parents and medical men, with rubeola and also with certain roseolas. Also there are erythemas which resemble the exanthem of measles and which are of gastrointestinal origin. In a healthy infant an eruption may suddenly appear, beginning, as in measles, on the neck. It may also occur on the trunk. There is no fever, malaise, or catarrh. There is, however, gastric disturbance, loss of appetite, furred tongue, fetid breath, and sometimes diarrhea. The writer draws attention to the importance of recognizing this condition in epidemics of measles, when a wrong diagnosis may be easily made. Raymond (Jour. des Mal. Cutan. et Syph., Nov., 1903).

Erythema vaccinium occurs during the course of vaccination. It may appear early, during the first two days, or may be delayed until the sixth or seventh, or at the time of beginning ulceration. Many patches of macules may be found over the body surface, with here and there an isolated macule of a bright-red color.

Erythema diphtheriticum is the form of disease observed in connection with diphtheria, in both mild and severe cases. (See DIPHTHERIA.) It appears sometimes as late as the second or third day of the diphtheritic process, and may occupy the trunk or extremities only, or may cover the greater portion of the body. The lesions are a diffuse redness of a mottled, punctate, or scarlatinal form, and when in patches it is generally located upon the thorax and abdomen, though frequently upon the extremities. According to A. R. Robinson, it does not usually increase in size after the first few hours and disappears during the next twenty-four or forty-eight hours without leaving any desquamation.

Erythema Choleraeium.—According to Duhring, there is an erythematous eruption observed in cholera patients. It occurs in polymorphous manifestations. These are usually macular, maculopapular, or papular, and are noted upon the dorsal surfaces of both the hands and feet, forearms, legs, face, and trunk. It may appear either at the beginning or termination of the disease and disappears in the form of a desquamation.

Erythema also occurs at times in *uremia, Bright's disease,* and *jaundice.* According to both Le Cronier Lancaster and H. Pye-Smith, lesions are observed. In uremia the lesions usually occur during the later stages of the disease and just shortly before the patient's death. They are at first erythematous, and in a few days become papular; fresh erythematous and papular lesions may afterward be observed at different stages of development over portions of the body. The lesions appear upon the extensor surfaces of the hands, forearms, and legs, and when numerous are noted upon all portions of the body, including the palms of the hands, soles of the feet, and mucous membranes, and are especially well developed upon the face. Upon the face they tend to become confluent and cause great disfiguration. They are bright red, and beyond a slight deepening of tint remain as noted for three or four days. They disappear either as flaky desquamations (often being as large as those noted in exfoliative dermatitis), hemorrhages being noted in the papules either during or previous to this stage, leaving a red, brawny, thickened skin; or it may become eczematous and terminate in the formation of crusts or in the formation of pustules and abscesses. Itching sometimes accompanies this condition.

Pathology.—The erythemas are the result of disorders of the vascular system and particularly those of the smaller vessels contained in the upper layers of the corium, and which radiate from there to the strata of the epidermis. Hyperemia is but an excess of blood propelled into the smaller capillaries through vasomotor action. The hyperemia differs with the character of the exciting agency. Transitory hyperemia caused by a slight injury generally fades quickly and no trace of its existence can afterward be determined, while those due to more marked lesions fade less quickly. Pressure leaves no visible change, though less pliability may be noticed. At first, in the active hyperemias, the skin may be of a lighter hue, but in passive hyperemia it becomes darker. Although the temperature is somewhat above that of the normal, it may not even effect or may even be slightly below that of the natural state.

Prognosis.—The prognosis of simple erythema is usually favorable. A slight hyperemic process, unaccompanied by inflammation, quickly subsides, although some degree of pigmentation may remain to mark its site.

Treatment.—When simple erythema is likely to disappear spontaneously, it is hardly necessary to advise any form of treatment, but in protracted cases, as well as those attended by recurrence, active measures should be resorted to. **Dietetic errors** should be **corrected.** Any intestinal irritant should be promptly removed by **cathartics.**

Rashes in children due to gastrointestinal disorders usually yield to fractional doses of **calomel.** In cases attended by tingling and burning or where a slight degree of exudation has taken place the application of some bland powder, simple lotion, or unguent will easily mend matters. **Boric acid,** either as a plain **powder,** in full **or** diluted strengths, a lotion in half or full saturated **solutions,** or as an **ointment,** ½ dram (2 Gm.) of **boric acid** to the ounce (30 c.c.) of ordinary **petrolatum,** will usually suffice. **Lycopodium** or **fullers' earth** will serve a similar purpose. At times it may be advisable to add a slight quantity of **carbolic acid** to procure early relief.

Schamberg recommends the following cooling lotion:—

℞	*Acidi carbolici*	♏xxx (2 c.c.).
	Acidi borici	ʒj (4 Gm.).
	Glycerini	fʒij (8 c.c.).
	Pulv. zinci oxidi	ʒj (4 Gm.).
	Aquæ	q. s. ad f℥vj (180 c.c.).

M.

ERYTHEMA SCARLATINIFORME.—Erythema scarlatiniforme (named by Hardy), roseola scarlatiniforme (Bazin), or erythema scarlatinoides (Besnier), is an erythematous skin eruption closely resembling that observed in scarlatina, and from which affection it must be differentiated.

> The writer's streptococcus vaccine can awaken an erythema resembling in every respect that of scarlet fever. As the streptococci are killed before the individuals are inoculated, the facts observed demonstrate for the first time the existence of a specific streptococcus toxin. The writer's experiences at Moscow with large numbers of children, showed that none of the other curative sera induce the production of the scarlatinal eruption, and still less the combination of sore throat, vomiting, raspberry tongue, etc., characteristic of scarlet fever, which follow inoculation with the streptococcus vaccine. The "vaccination scarlet fever" is distinguished from true scarlet fever by its milder and more rapid course and by the absence of contagion to other individuals Gabritschewsky (Berl. klin. Woch., Bd. xliv, Nu. 18, 1907).

Symptoms.—According to French dermatologists, there are two types of this affection. The one "érythème scarlatinoide," an acute rash resembling either scarlatina or measles, and accompanied or not by desquamation; other "érythème desquamatif scarlatiniforme récidivant," a subacute erythematous outbreak, resembling very closely scarlatina, usually accompained by desquamation. As its name implies, it is a recurrent affection.

In the more acute type the lesions may be preceded, from a few hours or two or three days, by some constitutional disturbance, notably malaise, with chilly sensation and a rise of temperature of two or three degrees. The lesions, which are of a pinkish-red or crimson color, are punctate or diffuse and situated on the chest, thighs, face, neck, and other regions, although they are not particular to any region. At times there may be slight itching or burning. The duration varies from a few days to one or more weeks. Aggravated acute types may desquamate either as thin, flaky scales or in large-sized exfoliations. Observers refer to still another type in which the affection simulates more particularly these characters of rubeola.

In addition to the general malaise, subacute cases are likely to present some disturbance of the renal functions and albuminuria. The lesions are rather more lasting and exist from periods varying from three to six weeks. When the eruption reaches its height there may be a lowering of the fever. A marked symptom of this variety is the number of recurrences, while desquamation is a prominent character. Hartzell refers to the diminution of severity with each succeeding attack.

Diagnosis.—Owing to the great resemblance of this affection to the rash of scarlatina, it is important that a close differentiation be obtained. The symptoms of the latter affection may present characters—such as the strawberry tongue, sore throat, great depression, and the presence of large or small quantities of albumin in the urine—which will usually be sufficient for all practical purposes.

The early desquamation or the desquamation during the height of the fever will generally serve to establish the nature of the affection present.

Etiology.—It may be the expression of forms of stomachic disturbances, such as produced by the ingestion of toxic agents, as alcohol, antipyrin, belladonna, copaiba, arsenic, opium, the iodides, salicylates, or carbolic acid.

Typhoid fever, surgical operations, rheumatism, parturition, certain infectious affections, and sewer-gas poisoning (Crocker) are among the numerous conditions which may give rise to the disease.

Pathology.—Why so many different avenues should lead to the same result is difficult to determine. Idiosyncrasy may play a very important part in assisting its appearance. Brocq has advanced the idea that the desquamative or subacute variety, as previously noted, is only a benign form of pityriasis rubra, but this theory has not obtained many followers.

Prognosis.—Serious consequences are unlikely to follow if produced by some form of irritative ingesta. Elliot states that the affection "is grave and indicative of death when it appears in the course of a pyemia, a septicemia, or a puerperal peritonitis." The relapses may be more or less numerous and a different cause may be ascertained in some cases for each recurrence.

Treatment.—The first indication is the removal of the inducing cause where possible. Should this be some form of irritative ingesta the use of **catharsis,** especially salines, may suffice. The local symptoms should be relieved by means of antipruritic or stimulating washes. **Boric** and **carbolic acids** (Schamberg's lotion for erythema simplex, *vide supra*) are probably the best remedies of this class. It may be deemed advisable in many cases to use more active local measures. For this purpose some active drugs, such as **menthol** or **thymol,** may be used.

Cases of erythema scarlatiniforme superposed on typhoid fever, show marked improvement under **epinephrin,** while conditions became aggravated whenever the epinephrin was suspended. Hutinel gives from 6 to 10 drops a day of the 1:1000 solution. In 1 case he kept up this dosage for several weeks with benefit and without by-effects. If it does not seem to be benefiting the child, he soon drops it.

> Case of typhoid fever in a boy of 12 years, who presented a scarlatiniform erythema on the knees, elbows, and buttocks, besides a leaden tint, a bad facies, ulcerated lips and nostrils, congestion at base of left lung. delirium alternating with extreme prostration, a very grave case in fact, contrary to the run of cases in children, which are generally favorable. The treatment was **cold baths** (32° C. —89.6° F.), every three hours, **cold compresses** on the abdomen, **hypodermic injections of camphorated oil,** and every day a dose of **adrenalin,** 1:1000, 8 drops divided into two doses. Even Hippocrates knew the danger of erythematous eruption in the course of an infectious fever, but its gravity has escaped the attention of many modern pathologists. It may be morbilliform or scarlatiniform in character and is usually accompanied by the excoriation of lips or nostrils, a lesion which will infect the skin of the finger if the patient touches it. Great prostration and adynamia are characteristic and death is the usual termination. Similar erythemata appear in the course of other infections and are always a grave sign. They

> must not be confounded with drug rashes. The autopsy in such cases discloses an enlarged liver with fatty degeneration; the renal system is also affected; the heart is often soft and discolored; the suprarenal capsules are enlarged and increased in weight; occasionally the thyroid and the pancreas are also altered. Fortunately adrenalin had a marvellous influence in the case under discussion; its remission was marked by a recrudescence of the symptoms, its renewal by their removal. It may be given for several weeks without danger, but should be watched. Hutinel (Presse méd., March 13, 1912).

ERYTHEMA INDURATUM SCROFULOSORUM.—This condition was first described by Bazin under the title "érythème induré des scrofuleux." It is an affection that may be mistaken for erythema nodosum. It is found in those persons of strumous diathesis and especially women and young girls (Crocker) who are easily fatigued and who are obliged to remain for long periods in a standing position.

It generally presents itself upon the anterior surface of the legs and occasionally upon the calf (Crocker); the lesions may be deep-seated nodes or nodules, which are either absorbed or break down into suppurating ulcers. In color they are first of a bright red, but they soon become darker or of a livid tint. After breaking they are observed to be punched out, round or irregularly oval ulcerations which resemble to a marked extent gummatous lesions.

In differentiating the early characters from erythema nodosum the acute and shorter course observed in the latter affection is to be noted. It may usually be identified by means of the tuberculin test.

> Case of erythema induratum of Bazin in a young woman aged 17 years. Her family history was negative with regard to tuberculosis. The patient was a healthy-looking young woman. Since childhood she had suffered from a weak peripheral circulation and chilblains. The characteristic lesions of Bazin's disease were present on both legs.
>
> On March 19, 1909, an injection of 1/10 mgm. of the **old tuberculin** was given, and as a result of this a slight general reaction occurred but no local reaction. Two days later an injection of 2/10 mgm. was given, which was followed by a marked general reaction and a local change, consisting of swelling, edema, and redness of the lesions. Some days later, at the site of the injections on the arm, two red, painful swellings about the size of five-mark pieces developed. These gradually disappeared, leaving pigmentation.
>
> The histological appearance showed that the affection was essentially a vascular lesion. The vessels were dilated and surrounded by a cellular infiltration. In places the endothelium had proliferated and a thrombosis was observed. Considerable numbers of giant-cells were present, and in places caseation and necrotic changes were noted. G. A. Gavazzeni (Monats. f. prakt. Derm., Sept., 1909).

Diagnosis from syphilitic gumma is established by its longer duration before the occurrence of ulceration, and the serpiginous outline of the latter, or the presence of scars.

Treatment.—The treatment is that of struma: **tonics, codliver oil, nutritious food,** and **out-of-door life.** Small doses of **thyroid gland,** not more than 1 grain (0.065 Gm.) three times daily in an adult may prove helpful. Where prolonged standing cannot be avoided, a well-applied **bandage** should be worn.

ERYTHEMA EXUDATIVUM MULTIFORME.—Erythema exudativum multiforme is an acute inflammatory and exudative affection of the skin, characterized by the appearance of macules, papules, or vesicles, discrete or confluent, and of varying sizes and configurations.

Symptoms.—The character of lesion observed, with its many configurations, has given rise to the use of certain terms which are indicative of the condition present: erythema multiforme papulosum is used when the predominating lesion is of the papular type; erythema multiforme tuberculosum when the size of lesion is slightly greater than the papule; erythema multiforme vesiculosum when of the vesicular type;

erythema multiforme bullosum when bullous; erythema multiforme annulare seu circinatum when it assumes an annular or rounded form; erythema multiforme figuratum seu gyratum when peculiar irregular lesions are formed from a coalescence of two or more annular or circinate rings; erythema multiforme iris when new lesions appear successively in the clearing center of preceding manifestation; erythema multiforme vesiculosum circinatum (herpes circinatus) when the borders of a papule are covered with a ring of vesicles; erythema multiforme vesiculosum iris (herpes iris) when several concentric rings of vesicles are formed; erythema multiforme urticatum (lichen urticatus) when from the edema they closely resemble urticaria.

> In Osler's group of 29 cases of erythema multiforme with visceral lesions, the number of symptoms present in any given case varied between four and ten. Purpura was noted in 22 cases, urticaria in 17 cases, edema in 5 cases, erythema in 14 cases, fever in 14 cases, colic in 25 cases, vomiting in 15 cases, diarrhea in 5 cases, hemorrhages in 14 cases, nephritis in 14 cases, albuminuria in 15 cases, arthralgic pains in 17 cases, endocarditis in 3 cases, and enlarged spleen in 3 cases. Various other manifestations were noted in one or two cases only. In the first case there were edema, erythema, fever, colic, vomiting, hemorrhages (from the kidneys), nephritis (including the albuminuria, classified separately in Osler's article), arthralgic pains, and enlarged spleen; in the second case, purpura, edema, erythema, fever, hemorrhage, arthralgic pains, and the group of symptoms relating to the nervous system, coma, hyperesthesia, photophobia, etc. Hall (Boston Med. and Surg. Jour., Sept. 3, 1908).

Erythema exudativum multiforme has points of predilection. For the most part lesions are observed upon the backs of the hands and feet, the forearms, and the legs. Next in frequency they occur upon the region of the head, the cheeks and neck, and lastly upon the trunk, the chest and back, and the abdomen. In aggravated cases, or in those unusual types, the lesions may be observed in other parts of the surface. They are usually first noted upon the hands and fingers, and from these regions spread to other parts, and result in some cases (as recorded by Duhring) in an enormous involvement of the whole general surface.

Death has been observed by Vidal and Leloir, and Molenes-Mahon speaks of a number in which death also occurred.

> *Appendicitis* as a visceral manifestation of erythema exudativum multiforme in 2 cases reported by the writer eight years ago. The matter of diagnosis is one of grave importance. The attack of colic, the so-called abdominal crisis of exudative erythema, may easily lead the inexperienced to make a diagnosis of appendicitis when no such lesion exists; on the other hand, a more serious mistake may be made of overlooking the coexisting appendix trouble, unless it is recognized that these vasomotor circulatory disturbances do at times result in congestion of, and even hemorrhage into, the appendix, with the result that there may be bacterial infection and inflammation or actual gangrene of this organ. The diagnosis of appendicitis in these cases must rest on the classical signs: pain, tenderness over the appendix, and localized muscular rigidity. That the erythema was not secondary to the appendicitis in the writer's case was clear from the fact that previous attacks of erythema had occurred and have occurred at intervals since the removal of the appendix. Chenoweth (Med. News, March 4, 1905).

Diagnosis.—The fact that death can occur from this affection renders an exact diagnosis of especial importance.

Eczema.—In papular eczema we may notice a symmetrical arrangement, but usually the lesions are regular as to size and outline. They may retain their appearance, but are prone to become either vesicles or pustles. Their duration is rather more lengthened, and crusting is likely to result from the excessive exudation.

Psoriasis.—Psoriasis is not likely to assume a symmetrical arrangement. It is more likely to be covered with decided desquamations and to be of much longer duration.

Tinea Circinata.—Circinate ringworm is not usually symmetrical, is slower in its extension, and more persistent in its character. The edges in this affection are usually well defined.

Syphilis.—Careful examination should be sufficient to make a correct diagnosis. The papular, and other varieties, will usually give some distinct sign of the syphilitic contamination.

Urticaria.—The lesions of urticaria are mostly uniform and of a white color, usually of short duration (rather evanescent) and are not likely to present different stages.

Pemphigus.—The lesions of pemphigus are bullous, always remain so, and depart as such, while they appear rapidly and are asymmetrical; they are not accompanied with much inflammation.

Dermatitis Herpetiformis.—In this affection the lesions are multiform (erythematous, vesicular, bullous, or pustular), are not symmetrical, and usually run a chronic course.

Erythema Nodosum.—The lesions are deep seated and nodular, are usually observed upon the lower extremities (along the tibia), do not change in appearance, and are painful (almost rheumatiform) at all times.

Etiology.—The cause or causes of this affection are obscure. It presents a tendency to recur at certain seasons of the year (usually the spring and fall), and is probably influenced by climatic changes.

Numerous cases are recorded in which the affection recurred at regular intervals, as, for instance, every year at the same time, every three months, at intervals of six or more months, or at longer stated intervals. All ages are affected, and the disease seems to more greatly attack young children and young females. There is no doubt but that certain affections predispose to its appearance; thus rheumatism, gout, uremia, Bright's disease, jaundice, diphtheria, and cholera.

> Case in which when the pregnancy had been of a few weeks' duration had a severe attack of erythema multiforme, the lesions in the early parts of the outbreaks being papular and erythematous, later of the iris form and vesicular, and finally bullous. This eruption persisted during four entire pregnancies, and continued for from four to eight weeks *post partum.* Three of the attacks have been personally observed by the writer.
>
> Treatment, save in so far as it alleviated the pruritus and protected the denuded surfaces, has not been of much effect. On the other hand, termination of the pregnancy and of the post-partum metabolic processes appear in each case to have stopped the outbreak. Gottheil (Amer. Jour. of Obstet., April, 1910).

Certain drugs taken internally may alike be mentioned as a possible influence.

Pathology.—Erythema multiforme begins essentially as an hyperemia, and is quickly converted into an exudative inflammatory disorder. It can hardly be classed as an essential and specific disease, a fact which some authors claim if we can really believe that so many diverse conditions will produce it. There is no doubt but that we have in the process an angioneurotic element, as claimed by Schwimmer, Lewin, and Auspitz. Many others have observed micro-organisms in the blood and lesions.

Prognosis.—All cases tend to rapid recovery, although a number of relapses may occur. Deaths have been recorded, but when the large number of cases is taken into consideration this loss of life is very small.

Treatment.—Internal treatment is to be directed toward the **removal of the exciting cause** where possible. All intestinal irregularities are to be remedied. **Calomel** is often efficacious as hepatic stimulant. Intestinal antiseptics such as **salol, sodium salicylate** and **creosote carbonate** are often helpful. Any tendency to rheumatism must receive attention, and **potassium iodide,** recommended by Villemin, may be found of good service, 15 to 30 grains (1 to 2 Gm.), thrice daily, as an absorbent in the vesicular and bullous form. Elliot says that it may, if given injudiciously, provoke an aggravation of existing conditions. In this class of cases, Atkinson, of Baltimore, relies upon **salicylic acid** and the **salicylates.** Cantrell frequently obtained excellent results with **arsenous acid** given during and between attacks.

> Case of erythema multiforme, in a woman aged 27, that had existed from childhood, occurring every fall and disappearing in the winter. Intramuscular injections of ¾ grain (0.048 Gm.) of **cacodylate of soda,** given twice a week for several weeks, completely relieved the attack. Each injection was followed by relief and the disease disappeared entirely, leaving her in better condition, according to her own statement, than she had ever been in since it first occurred. From his experience in this case the writer would recommend cacodylate of soda injections for trial in all cases of erythema, more especially in the angioneurotic type. W. Cuthbertson (Jour. Amer. Med. Assoc., Jan. 6, 1912).

Quinine is certainly demanded in those types which are presumably the effect of malaria. Antistrumous remedies—such as **codliver oil, phosphorus,** and possibly **strychnine**—in those debilitated by such processes are valuable in the tubercular forms.

Local measures, while possibly directed alone to the relief of subjective symptoms, may also be found beneficial. **Boric acid** is of distinct value in this affection, and applied in a saturated watery solution gives almost instant relief from the itching and burning that are occasionally observed. Schamberg recommends the following as a sedative and antipruritic lotion:—

℞ *Resorcini* .... ʒj (4 Gm.).
Acidi borici .... ʒj (4 Gm.).
Glycerini .... fʒj (4 c.c.).
Zinci oxidi .... ʒij (8 Gm.).
Spirit. vini rect. .... f℥j (30 c.c.).
Aquæ .... q. s. ad f℥ij (60 c.c.).
M. Sig.: Apply frequently.

The **sulphite** or **hyposulphite of sodium** may often be used advantageously in the strength of from ½ to 1 dram (2 to 4 Gm.) to the ounce (30 c.c.) of water. **Ichthyol** may be found of service in the vesicular and bullous types. At times stimulating remedies may act efficaciously, especially **salicylic acid, carbolic acid,** and **sulphurous acid,** in varying strengths of solution.

In the urticarical type antipruritic lotions such as the above may be demanded. Mild cases may not require treatment, the subjective symptoms being very slight.

> Many striking illustrations of the beneficial effect of a restriction of nitrogenous food under certain conditions are found in the use of the so-called **"rice diet,"** which included hot boiled rice and bread at least twenty-four hours old. In severe erythema multiforme, in various acute inflammatory affections, in recurrent vesicular eruptions of the hands, in some eczemas, in the acute exacerbations of psoriasis, and in severe rheumatoid arthritis, the "rice diet" caused a complete cessation of distressing symptoms and a disappearance of the lesions. L. Duncan Bulkley (Trans. Amer. Med. Assoc.; N. Y. Med. Jour., June 15, 1912).

ERYTHEMA NODOSUM.—Erythema nodosum is an acute inflammatory affection of the skin, characterized by the appearance of symmetrical, elevated, variously sized, shaped, and colored nodular formations, accompanied by constitutional disturbance.

> Outbreak of erythema nodosum in a home for children. There were 13 cases in all; 1 of them was followed within twenty-four hours by symptoms of meningitis, ending in death two and a half days after the onset of the erythema; another patient became profoundly ill, temperature going to 104° F. (40° C.); 4 developed endocarditis as a part of the infective process; 4 of them had relapses. The outbreak emphasizes the following facts: erythema nodosum may become a serious and dangerous disorder; it is sometimes epidemic; it appears to be of an infective nature; endocarditis may arise during its course; it may be quickly followed by meningitis. W. Langford Symes (Brit. Jour. of Children's Dis., vol. xiv, p. 281, 1907).

Symptoms.—Preceding the appearance of the lesions of an erythema nodosum there is usually general constitutional disturbance. Chills, with an elevation of temperature, or myalgic or rheumatic pains may be encountered. According to Duhring, edema may be one of the first symptoms, while visceral involvement—with, later on, lesions of the heart and kidneys—may be present. For the most part, the nodes are localized upon the anterior surface of the shins, along the line of the tibiæ, and are arranged symmetrically. They are also observed, in exceptional instances, upon other parts, the arms, face, and chest, along the line of the ribs, and upon the abdomen. Pospelow, quoted by Elliot, noted similar involvement of the mucous membranes of the mouth These nodes appear rather suddenly, developing rapidly, and are of a light or rosy red color, but later become darker in appearance, of a bluish or of a purplish tint. Appearing either singly (usually) or in crops, the process may extend over a period of from one to five weeks (or longer), although each individual lesion lasts only about six or eight days. While disappearing they assume various colors, from a yellow to blue or purple, and closely resemble a bruise. During their height they have a tense and shiny look, and give to the touch an indistinct impression of containing fluid. They rarely suppurate, absorption generally taking place, although this result has been observed by Haisholt and others. Dilatation of the capillaries has been observed by Lewin and Unna, while Van Harlingen has noted lymphatic involvement. Hemorrhage has, according to Demme, been observed in a case in which gangrene also took place. They are always painful and at first are firm to the touch, although they soon become softer, as they are disappearing. Some authors have described an ominous form of the affection in which tuberculosis is noted. Occasionally erythema nodosum and erythema multiforme are coexistent, especially that variety of erythema multiforme in which papules are the predominating manifestation.

> Erythema nodosum following measles in 9 out of 300 cases. In most of the cases about ten to fourteen days had elapsed since the first onset of measles before the erythema nodosum made its appearance. In half the cases the first symptom was pain in the joints, followed by the erythema in about twenty-four hours. There was no history of rheumatism or contact with rheumatic fever in any of the cases, and no rheumatic or cardiac lesions were found in any of the patients. The question of sore throat before or at the time of the measles rash was carefully gone into by the writer, but it was present in 1 case only. Joynt (Brit. Med. Jour., April 15, 1911).

Diagnosis.—While with a careful survey of the lesions presented, as well as the concomitant phenomena, little cause may exist for error in diagnosing erythema nodosum, some instances do occur in which difficulty may be experienced.

Contusions are likely to be single and do not present those deep nodular formations. The cause can generally be determined.

Syphilis.—The syphilitic gummata, especially the non-ulcerating variety, which often resemble erythema nodosum, are sharply defined, indolent, and occasion no pain.

Erysipelas generally presents a hard, though diffuse, inflammation, instead of a more circumscribed character of swelling.

Erythème induré des scrofuleux is not painful, is asymmetrical, of longer duration, and tends to ulceration; occurs in scrofulous subjects.

Etiology.—Erythema nodosum is an affection of early life, although instances in which it has affected varying ages have been recorded. Out of a total of 108 cases, S. Mackenzie found 14 under 10 years of age, 69 between 10 and 30, 15 between 30 and 40 years, and 10 over 40 years of age. Comby has presumably recorded the youngest, 14 months old. Most authors consider that the spring and autumn contribute the greatest number. Rheumatism accompanied many cases. Malaria was found to be a possible exciting cause by Boicesco.

> Six cases of erythema nodosum with exudation affecting the mouth or upper air-passages, occurring in persons years after syphilitic infection. The writer believes that the syphilis was not directly responsible, but merely afforded the predisposition for the development of the lesion. Mercurial treatment is unnecessary. In the cases reported excellent results were obtained with **potassium iodide,** and in every instance there was a prompt and salutary reaction to salicylic acid. Trautmann (Münch. med. Woch., Bd. liii, Nu. 43, 1906).

The arthritis which accompanies some cases of erythema nodosum is thought by most observers to be of rheumatic origin. The writer's own experience is that the signs or a history of chorea, endocarditis, or arthritis are not found in more than 10 per cent. of all cases of erythema nodosum. The disease differs from rheumatic fever further in that it more commonly attacks females than males, and is most prevalent in the autumn, winter, and spring, while rheumatism is most common in summer. A long period of prodromal malaise, comparative freedom from the risk of recurrence, slight constitutional disturbance during the pyrexial period, and the presence of phlyctenulæ in the eyes are also characteristic of erythema nodosum. The arthritis may differ entirely from that met with in rheumatic fever, and it, together with the pyrexia and rash, are but little influenced by the administration of salicylates. J. O. Symes (Brit. Med. Jour., July 27, 1907).

Cases of erythema nodosum occurring in tuberculous subjects or followed by tuberculosis have been reported from time to time, but this association has generally been regarded as accidental. The writer, in 6 cases of erythema nodosum, obtained positive reactions by a method of slight scarification and rubbing in of tuberculin. In 2 of these cases there were evidences of tuberculosis. One had signs of tuberculosis at the apex of one lung. The other, a boy, aged 7 years, reacted to the tuberculin test while the eruption was out; two weeks later he developed measles, followed by nephritis, which cleared up in three weeks, when he again gave a positive reaction; three months later he had hemoptysis and was found to have signs of tuberculosis in the lung, and again reacted positively. A. B. Marfan (Presse méd., June 26, 1909).

The resemblance between syphilitic erythema nodosum and Bazin's disease (erythema induratum) is becoming more and more apparent. The writer regards it as a malignant form of syphilis (precocious tertiary), which is frequently preceded, accompanied, or followed by gummata. Leviseur (Jour. Cutan. Dis., Nov., 1911).

Pathology.—Erythema nodosum is due to an inflammatory process, at first active and later passive. Atkinson, of Baltimore, argues that it is an overcrowding of blood- and lymph- vascular spaces and exudation of blood-cells, both white and red. The process affects the entire skin, and is believed by Kaposi to be a more fully developed and stable urticarial wheal.

Prognosis.—The prognosis is usually favorable. Relapses may occur or the process may be extended by successive outbreaks of new lesions. The usual length of each attack is from one to five weeks, although the individual lesions usually run their course in from six to eight days. Death has been recorded, but this is exceptionally rare.

Treatment.—The disease tends spontaneously toward recovery, and it is very highly probable that constitutional measures exert little influence. General disturbances of the constitution require appropriate attention. A bland **diet** should be advocated and **rest** in bed advised. **Iron, quinine, phosphorus, acetanilid,** and **phenacetin** are often beneficial. To reduce inflammation, relieve pain, and prevent complications, a solution of **sulphite** or the **hyposulphite of sodium** in water, 1 dram (4 Gm.) of either to the ounce (30 c.c.), will be found useful. **Ichthyol** has also been of service in many hands (1 dram—4 Gm.—to the pint—500 c.c.—of water). **Phenol, sulphurous-acid** solutions, **lead water** and **laudanum, boric acid,** and **hot fomentations** may also be mentioned as useful remedies when the others mentioned fail.

Erythema nodosum may be secondary to some affections where tuberculosis can be excluded, and also evolving secondarily during well-marked tuberculosis, the latter being by far the commoner; secondly, it may be primary in appearance, and even benign, but the greater number of cases arise from a tuberculous soil, which is not at first apparent, but shows itself later. The writers recommend **rest** in the horizontal position in bed, **wet compresses** of water, slightly alcoholic, and covered with absorbent wool. If the pain is very severe, apply petrolatum 40 Gm. (1½ ounces), extract of **belladonna** 0.50 Gm. (7½ grains), and extract of **opium** 0.25 Gm. (4 grains) as an ointment, and cover the limb. **Sodium salicylate** and **potassium iodide** are of value. If signs of tuberculosis are present, **open-air** treatment is advisable and good food and hygienic conditions. Deléarde and Hallez (Brit. Med. Jour., Oct. 7, 1911).

C. and S.

ERYTHRASMA. See Pinta.

ERYTHROLTETRANITRATE is a polytomic organic nitrate which, as do all bodies of this class, detonates when struck with a hard body. In this particular it is even more sensitive than guncotton or dynamite. Its dangerous activity may be developed when gently stirred with apparently harmless compounds. An explosion of erthyrol-tetranitrate cost Mr. Lewis Jones, a qualified chemist, his life. Mr. Jones was engaged in stirring together in a mortar a mixture of erythrol-tetranitrate and lactose, presumably for the purpose of making tabloids. The quantity of the active drug served out to him was 4 ounces.

Bradbury holds that the drug is perfectly safe unless rapidly heated or struck or mixed with some readily oxidizable substance.

Erythrol-tetranitrate is solid and crystalline, and melts at a temperature of 61° C. (142° F.). When pure it is colorless, and if kept in a dark and moderately cool place is fairly stable. If exposed to warmth, and especially sunlight, it rapidly undergoes decomposition, turning yellow and giving off nitrous fumes.

PREPARATIONS AND DOSE.—The dose of the solid nitrate is ½ to 1 grain (0.03-0.06 Gm.). It can be given in pill, tablets, or in alcoholic solution. Its solubility in water is slight, but it dissolves readily in alcohol and in ether.

PHYSIOLOGICAL ACTION.—It is a vasodilator, and belongs to the group of which glycerol-trinitrate, known familiarly as nitroglycerin, may be regarded as the typical representative. Its action is slower and more lasting than that of nitroglycerin, beginning in about fifteen minutes and lasting for three to four hours. Blood-pressure experiments show that the nitrates of erythrol and mannitol have a less marked, but more prolonged, action than glycerol and glycol.

THERAPEUTICS.—Bradbury speaks highly of its therapeutic properties in warding off attacks of **angina pectoris** and in keeping down arterial tension in chronic **Bright's disease.** In the former disease it is sometimes necessary to avert the paroxysms, to administer the remedy in steadily increasing doses. Garaway treated a case in which the patient finally took ½ dram (2 Gm.) in the day: that is, 6 grains (0.4 Gm.) at 6 A.M., to enable him to dress at 8 A.M.; 6 more at 10 A.M., 2, 6, and 9 P.M., together with 1/25 grain (0.0027 Gm.) of trinitrin at 10.30 P.M. to enable him to ascend the stair and get to bed. This kept him in perfect health, barring the seizures, which are always at hand, if a tabloid chance to be omitted. No physiological effects whatever were at any time manifested. Walsham used it with good results in **aortic regurgitation,** accompanied with cardiac pain, and also in **Raynaud's disease.**

S.

ERYTHROMELALGIA. See Vascular System, Disorders of.

ESERINE. See Physostigma.

ESOPHAGUS, DISEASES OF.—MALFORMATIONS.—*Congenital occlusion,* due to the fact that during embryological development the invagination forming the mouth fails to open into the posterior end of the primitive intestine; *diverticula,* of similar origin, and *fistula* due to incomplete closure of the branchial clefts represent the main malformations met with in this region. *Congenital narrowing* due to abnormal thickness of the wall or to the presence of membrane or web and *congenital dilatation* are also, though very rarely, witnessed.

Case in which the patient had had trouble with swallowing for fifteen years. The examination disclosed, about an inch below the cricoid cartilage, a thin web which surrounded the esophagus. It was in the form of a diaphragm with a small central opening. The nature of the web did not become clear until the writer put the mechanical dilator through the aperture, spread the dilator and pulled it back a little. The manipulation put the whole diaphragm on the stretch and made its real character plain. After the diaphragm was put on the stretch, the ring of tissue was divulsed by pulling the dilator up. After this soft bougies were passed at intervals three times. The patient was quickly and easily cured. Mosher (Laryngoscope, Nov., 1911).

Three unusual cases of congenital stenosis of the esophagus. The symptomatology of the cases was very similar and consisted in the following: When fed, the baby choked and the mouth and throat seemed full of mucus. The child sucked and swallowed well, but after a few minutes strangled and the feeding came up again. The stool consisted entirely of meconium. A catheter passed into the esophagus was arrested about 10 cm. from the gums and could be passed no farther. The children lost weight rapidly and died. An autopsy obtained in one of the cases showed the lumen of the esophagus to end sharply about one-third of the distance from the epiglottis. From here downward a narrow band replaced the esophagus to just above the cardia, where it reappeared. In 4 other cases, in children who were respectively 11, 6, 3, and 5½ years of age, there was only partial obstruction of the esophagus. The first 2 were due to congenital narrowing, the third to cardiospasm, the fourth to hysteria. All vomited solid food immediately after swallowing, and had been fed from birth on liquids. X-ray plates of the first 2 showed the lesions, while the plates of the last cases showed no evidence of narrowing. J. L. Morse (Archives of Pediatrics, July, 1912).

PEPTIC PERFORATING ULCER.—This class of ulcer is rarely met with in the esophagus, but its recognition is very important owing to its serious nature.

Symptoms.—The most typical and constant symptoms of the condition are: Pain, which is severe and comes on immediately after food, the site of the pain being at the lower end of the sternum and a little to the left of it. Pain is also felt between the shoulders. Vomiting is the next most constant symptom. Dysphagia is present in more than half the cases. It is due to reflex spasm of the muscle of the esophagus from pain, and it is the main diagnostic point differentiating the condition from gastric ulcer. Hematemesis is also a very common symptom. (Miller.) The esophagoscope, carefully employed, may prove helpful in identifying this condition.

Etiology and Pathology.—Regurgitated gastric juice or islands of gastric mucosa aberrant in the mucosa seem to underly this condition. The ulcer is usually single. It may extend into the stomach, and independent ulcers may occur in the stomach or duodenum. The situation is usually close to the cardiac orifice, and the right posterolateral wall appears to be the commonest site. The condition is usually found in middle life. As regards sex, of 45 cases in which the sex was specified, 31 were males and 14 females. This preponderance of the ulcerations in the male corresponds to what one knows of duodenal ulcer.

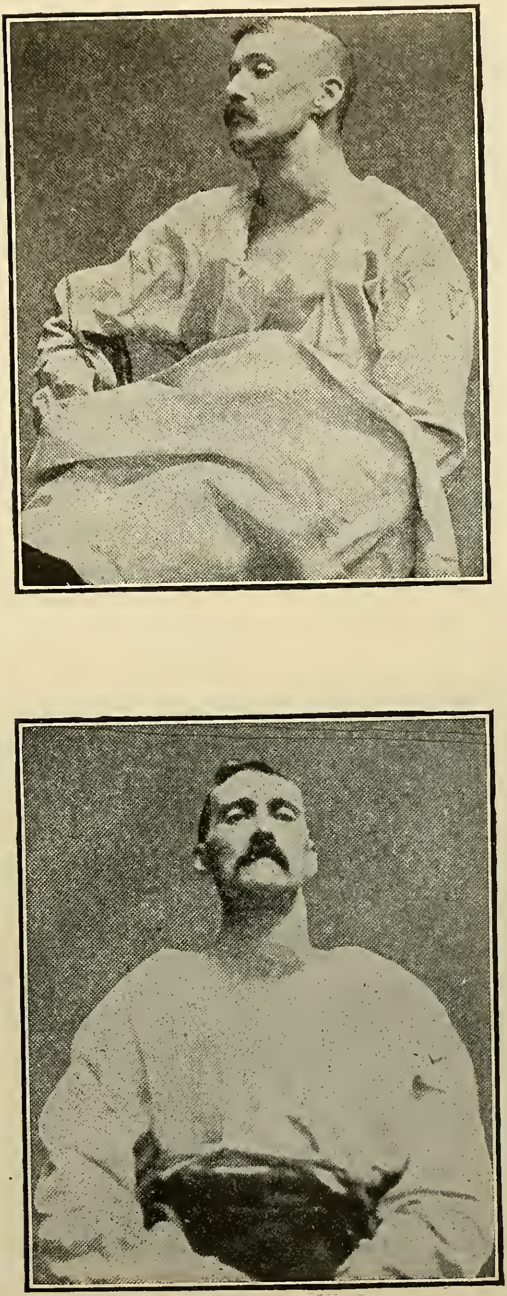
Personal case and 14 on record in which the peptic ulcer was confirmed by autopsy. None of the cases had been correctly diagnosed. This is not surprising, as in only 5 cases were there any symptoms in the esophagus, pains or difficulty in swallowing, and in 3 of these gastric disturbances predominated. Regurgitation of the gastric juice into the esophagus is favored by stenosis at the pylorus or duodenum or by hour-glass stomach in 7 cases, and in most of them the cardia is much enlarged. In 8 of the 15 cases there were coexistent gastric or duodenal ulcers. **Dietetic measures** should be instituted on suspicion of peptic ulcer in the esophagus or direct endoscopic local treatment. The most effectual measure, however, is prompt **gastrostomy** which rests the esophagus and gives it a chance to heal, thus warding off impending hemorrhage or perforation. Kappis (Mitteil a d. Grenzgebieten der Med u. Chir., Bd. xxi, Nu. 5, 1910).

Personal case in which there was an ulcer of the lower part of the esophagus perforating into the left mediastinum and left pleura. The autopsy showed an old tubercle at both apices, chronic ulcer of the duodenum, recent fibrous pericarditis, and cloudy swelling of various organs. Miller (Brit. Med. Jour., Jan. 20, 1912).

Two cases of peptic ulcer of the esophagus. The ulcer in the first case perforated into the left pleura; in the second case no perforation occurred. In the first case a diagnosis of perforated gastric ulcer was made, and in the second a diagnosis of gastric ulcer. In both cases acute abdominal symptoms occurred; laparotomy was performed, and nothing abnormal was discovered. Both cases ended fatally. C. G. Watson (Brit. Med. Jour., Nov. 2, 1912).

Treatment.—As peptic ulcer of the esophagus is generally secondary to some lesion elsewhere, the latter demands attention. The ulcer itself requires the same treatment as gastric ulcer, as to drugs. **Bismuth** insufflated through an esophageal tube may serve also as an excipient for **morphine** or **cocaine** to counteract the pain, which is usually severe. Applied a few minutes before meals, such a combination facilitates greatly the ingestion of food, thus counteracting the tendency to emaciation. Silver nitrate should be avoided in these cases, as it tends to encourage the formation of cicatricial bands and therefore to produce stenosis. After the ulcer has healed careful **dilatation by** means of **esophageal bougies** is necessary. In some cases, **surgical measures** become **necessary.**

Case of **ulcer in** the esophagus, 2 cm. above the cardia, which first revealed its presence by symptoms of perforation and acute peritonitis. As it proved impossible to suture the perforation and the patient was almost moribund, he drew up the fundus of the stomach and wrapped it around the lower end of the esophagus, holding it in place by a few sutures 5 or 6 mm. beyond the perforation. The peritoneum was filled with a grayish, odorless fluid, but he drained it away and introduced besides into the peritoneum a large tube through a buttonhole in the iliac fossa on each side. The operation was completed in fifteen minutes and as soon as the patient had been returned to bed, half sitting up, the writer connected one of the iliac fossa tubes with a tank of **oxygen,** thus flushing out the peritoneum with a continuous stream of oxygen, supplemented by **proctolysis,** flushing the rectum with a continuous stream of hot **saline solution** through a two-way tube, and the ordinary stimulants. The patient was a woman of 25 and her condition was very precarious for twenty-four hours, but then she rapidly improved and the oxygen was discontinued the sixth day. The eleventh day the temperature rose a little and very little pus escaped through the drains; so he connected one tube with the



Esophageal diverticulum resembling parenchymatous goiter. (*William Robinson.*)
(Practitioner.)

oxygen tank again, and pus poured anew out of the drains. The oxygen was discontinued the fourth day and the patient left the hospital in good condition the thirtieth day after the operation. The author makes a point of connecting each of the drain-tubes in turn with the oxygen tank, extolling this continuous flushing with oxygen as a most important aid in **drainage.** It is, he says, a physiological antiseptic which exalts the defensive powers of the peritoneum, combats paralysis of the viscera, promotes peristalsis, and has a stimulating action on the circulatory and respiratory apparatus. Of his 12 patients with diffuse septic peritonitis treated with the oxygen he was able to save 6 and still another recovered from the diffuse peritonitis, but succumbed later to an unsuspected complication. His proportion of recoveries has thus increased from 29 to considerably over 50 per cent. L. Sencert (Archives gén. de chir., Nov., 1911).

PRESSURE DIVERTICULA (PHARYNGOCELES).

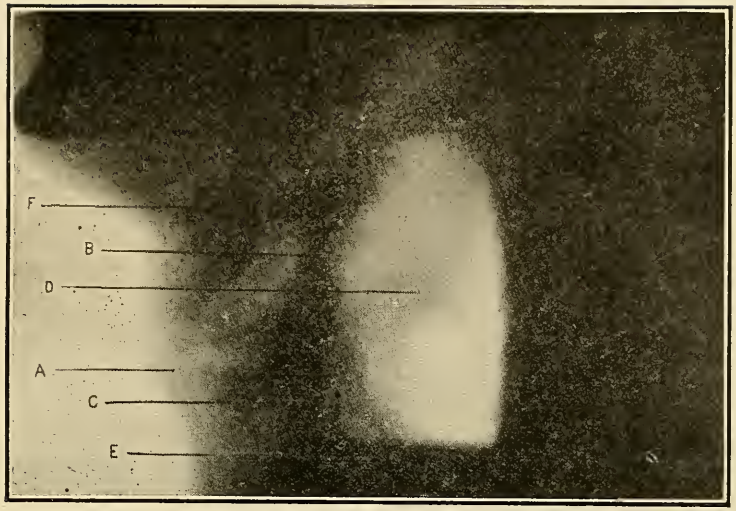
Symptoms.—A pressure diverticulum may occur as the result of inflammation or injury; the esophageal wall is weakened, a portion of it bulges out, forming a circumscribed sac, or hernia, through the muscular coat. While small, a pouch thus formed is hardly noticed, but, as small particles of food find their way into it, it is gradually enlarged, projecting downward. It may become several inches deep, is usually elongated, and appears externally as a pear-shaped growth between the larynx and the sternomastoid muscle. It may, by its pressure, displace the esophagus and the larynx, causing violent coughing through pressure upon the superior laryngeal and dyspnea. The external swelling may suggest a costic. (See cuts.) Dysphagia, fetor of the breath, regurgitation of ill-smelling masses of sodden food, and local pain are experienced in severe cases. Death from inanition has resulted.

Diagnosis.—A diverticulum may easily be recognized by palpation, especially when the patient is lying on his side, the tumor being upward. When it contains air, pressure upon it causes this to pass out and its size is reduced; when it contains food, pressure either causes marked lateral displacement of the esophagus or the food is forced up into the esophagus and mouth. It is often enlarged after meals. The sound may be used; it should be bent so as to enable it to enter the cavity, and be handled with great gentleness. (See annexed cuts.)

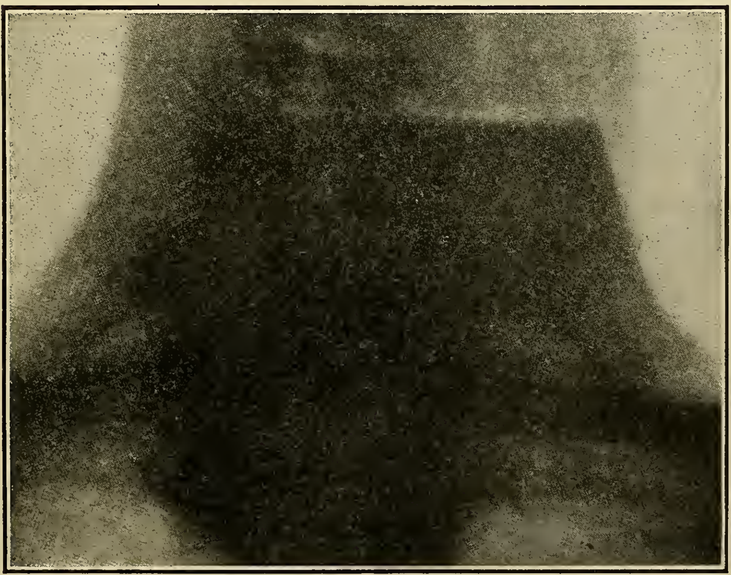
The examination should be conducted in a routine manner, the esophagoscope being used last, bearing in mind always the danger of a rupture of a possible aneurism. In making the examination with the X-ray, the introduction of a soft tube filled with shot (Mayer) may take the place of bismuth.

Etiology.—Inflammation and injury to the muscular coat are the predominating factors. It is usually observed in men, and at the spot where the pharynx ends to become the esophagus. The congenital forms are usually situated near the inferior constrictor.

Treatment. — The treatment of pharyngocele is essentially surgical, if cure is to be obtained. Interference with deglutition preventing adequate nutrition, the stomach-tube or rectal feeding must be employed as in dilatation of the esophagus. The great trouble with these cases is that decomposing food masses tend to pro-



Side view. *A*, larynx; *B*, pharynx; *C*, mouth of diverticulum; *D*, air in upper part of sac; *E*, upper level of bismuth pap in sac; *F*, hyoid bone.



Front view.

X-ray picture of large diverticulum. (*William Robinson.*) (Practitioner.)

duce inflammation in and about the sac; lavage of the latter is therefore of great need. It is done much as is that of the stomach, the tube being passed into the diverticula. The application of astringent and antiseptic solutions to the atonic mucosa is often of benefit, as is also the regular use of electricity by means of the esophageal electrode. Rest and general hygiene, which may have to be supplemented by the administration of sedatives and plentiful nourishment, should be insisted on. Fat is an especially important article of diet, and may conveniently be given in the form of melted butter or olive oil a short time before meals. The following are some of the foods which may be included in the dietary: Beef-juice, rich soups and broths, including those containing cream, eggs; purée of all vegetables which do not have tough fiber, among them being purée of spinach, beans, peas, celery, asparagus, and potatoes; milk and cream; cocoa, chocolate, coffee, and tea; eggs, raw or soft; scraped meat and fish chowder; porridge made from thoroughly cooked breakfast cereals; a few sweets, such as bees' honey, calf's-foot jelly, and simple custards.

> Where the diverticulum has not occasioned any symptoms beyond that of mild distress, we may content ourselves with occasional **washing** out of the **diverticulum** and care as to **diet**. Where, however, emaciation exists, the diagnosis having been firmly established, radical operation may be performed with success. Whether a previous **gastrostomy** should be done or not, must be decided for the individual case, but enough information is at hand to show that the operation for pharyngoesophageal diverticulum is readily performed and reasonably safe. Stetten has collected statistics of 60 radically operated cases; of these, 50 patients were cured and 10 died, a mortality of only 16.6 per cent. Mayer (Med. Record, July 2, 1910).

TRACTION DIVERTICULA.

This is a form of diverticulum which presents itself near the bifurcation of the trachea, in the anterior wall of the esophageal canal. It is generally associated with inflammation of the lymph-glands in this locality. Local inflammation followed by ulceration gives rise to cicatrices which by their contraction draw on the esophagus, *i.e.*, exercise traction upon it, forming a cavity opening into the esophageal canal by a funnel-shaped orifice.

Symptoms.—Mechanical irritation is occasionally produced by the retention of food, and ulceration may follow, attended by its usual complication—perforation. A fistula between the esophagus and the bronchial tract may be followed sooner or later by pneumonia.

The pleura and pericardium may also be reached. In the majority of cases the symptoms are slight; it is only on account of the possible mortal complications that traction diverticula demand attention. The X-ray and esophagoscope are as useful here for diagnostic purposes as in the form previously described.

Treatment.—**Surgical removal** alone affords protection against possible complications.

FOREIGN BODIES IN THE ESOPHAGUS.

Foreign bodies frequently become impacted in the esophagus, fish-bones, pieces of meat, pins, tacks, artificial teeth, coins, and buttons representing the class of articles found in the majority of cases.

Symptoms.—These vary according to the shape, size, and location of the impacted agent. A large mass, such as a piece of meat, may become engaged behind the larynx and hold the tip of the epiglottis down, completely closing the laryngeal cavity. Here, intense dyspnea soon comes on and death from asphyxia may promptly follow. Or a part of a bolus may invade the larynx and cause violent spasm; asphyxia again becomes possible from two causes: spasm and reduction or total closure of the respiratory area. Small bodies may produce the same symptoms, but, as is the case with large masses,—meat, bread, etc.,—they seldom give rise to dangerous symptoms, unless the larynx is involved by pressure, puncture, or the epiglottis is held down in some way.

> While it is true that the esophagus is occasionally very tolerant of such foreign bodies, perforation and death have followed sometimes within very short periods. The absence of symptoms of pain, difficulty of deglutition, etc., are not a safe index of the seriousness of the existing condition. The use of a sound for diagnosis is objectionable, as it frequently fails to reveal the actual state of affairs. In case of sharp foreign bodies the obturator should never be used with the esophagoscope, and in any case it is advisable to leave it out to permit inspection of the entire tract. It may be necessary to cut or break the foreign body before it can be extracted, and for that purpose Kahler's forceps are useful. If perforation has occurred and caused a periesophageal abscess in the cervical portion, the use of the esophagoscope is contraindicated. Such an abscess must be dealt with from without and as early as possible. If the foreign body has perforated the thoracic part and caused a mediastinal abscess, the esophagoscope is imperative before opening the mediastinum in order to determine on which side the abscess is located. To perform esophagostomy before trying to extract the body with the esophagoscope is not justifiable, as the operation has a considerable mortality. The writer illustrates an instrument of his own device for extracting foreign bodies and reports 5 cases in his practice, in all of which extraction was successfully performed and recovery resulted. He also gives an analysis of 200 cases reported in the literature since 1900, and sums up his conclusions in the following: "1. Esophagoscopy is not a difficult procedure and it gives the best results in the treatment of these cases with the least discomfort to the patient. 2. The use of instruments in the esophagus, except through the esophagoscope, in case of sharp foreign body, should be abandoned. 3. In every case in which the swallowed foreign body is not recovered an esophagoscopic examination of the esophagus should be made. 4. Even if the foreign body is successfully pushed into the stomach the patient is not entirely beyond danger." W. Lerch (Jour. Amer. Med. Assoc., March 4, 1911).

Sharp or irregular bodies,—such as chicken-bones, tacks, etc.,—when impacted only in the esophagus,—usually at its upper portion and immediately behind the cricoid cartilage,—only cause marked discomfort and severe pain, especially marked during deglutition; but they are attended with little or no immediate danger. The pain may radiate in various directions. Hemorrhage or rather slight bleeding is occasionally produced. After some time, varying with the size and shape of the body, the acute suffering ceases and pain is only experienced during deglutition.

If the impacted body is low down, which is frequently the case when it is small, it is only at this time that its true location can sometimes be established, the sensations before this being misleading. But the pain even at this time may only indicate the location of a lesion produced by a rough or sharp body during its passage to the stomach. Bronchoscopy and esophagoscopy are so important in this condition that they should always be employed when the location of the foreign body is at all in doubt or where it cannot readily be reached. The fluoroscope screen has also been used with profit.

It is remarkable that more general use is not made of bronchoscopy and esophagoscopy, while too much reliance is placed on roentgenoscopy, percussion and auscultation, and too little credence given the patient's statements. In three personal cases, the presence of the foreign body had been denied by previous examiners while direct visual inspection revealed it at once. One patient was an elderly man who applied for a "remedy for his cough;" only by persistent questioning was it finally learned that his cough had come on after he had "swallowed something the wrong way" some time before. Although there were no objective findings, yet the bronchoscope showed three slivers of bone which were readily removed. Reinking (Deut. med. Woch., Nov. 30, 1911).

In all cases in which a foreign body is either swallowed or inspired, a radiograph should be made by a competent person before any attempt is made at its removal. This is especially important in cases of sharp bodies. If the foreign body is dense enough to be revealed on a plate, the diagnosis by this means is easy; but even in those cases in which a vegetable foreign substance is not opaque to the Roentgen-ray, a great deal of information can still be obtained. A grain of corn, for instance, lodged in the bronchus will not cast a shadow on a photographic plate, but its presence can usually be determined by the slight changes in the lung itself, caused by a localized pneumonia, or by a blocking up of certain air-cells. The same is true of vegetable foreign bodies in the esophagus; for while the body itself cannot be seen, information especially as to its location can be obtained by giving the patient bismuth, either in the form of a capsule or in gruel, and watching the passage of the preparation down the esophagus with the fluoroscope. If a foreign body is present, the bismuth will be stopped or at least hesitate at the obstruction. Bowen (Ohio State Med. Jour., July, 1911).

Left *in situ*, foreign bodies always tend to create local lesions, unless, as sometimes happens, spontaneous expulsion occurs after the primary local irritation and the general excitement of the patient has ceased. Local inflammation is caused, the tissues become softened; abscesses arise which may burrow in various directions, sometimes reaching into the pleura, the pericardium, the mediastinum, or the larger vessels, including even the aorta. The foreign body itself may follow either of the channels formed and cause death by reaching any of the organs of the thoracic cavity. Needles particularly are prone to migrate in various directions and sometimes appear at a spot quite remote from the gullet and totally disconnected with it as to continuity of tissue.

A few patients having died from foreign bodies in the esophagus in the writer's service, some lessons have been derived therefrom. Among them is the necessity for examining the opposite side of the esophagus when the foreign body is removed from without. When it is large and has been impacted for some time the tissues are likely to be injured all around, and especially at both ends of the foreign body, so that the perforation may be double and infection may occur from the side opposite the incision. It is sometimes wise to open into the esophagus from the opposite side to explore the other side; the writer found this of great advantage in one case which certainly would have terminated fatally without it. The first point to be ascertained is the nature of the foreign body that has been swallowed, whether it has smooth or sharp edges. In one case the family related that the child had swallowed a cloth-covered button from her father's underdrawers, and as there was not much disturbance, and the child was able to swallow fluid food and did not seem much incommoded, while the Roentgen picture showed the button lodged not far down, several days were allowed to elapse while a suitable button catcher was being made, with which the button was finally safely removed. But instead of being as described, the button was of another kind and had sharp edges which had burrowed into the walls and the child died of sepsis two days later. Another lesson learned from his experience is that the Roentgen-ray examination should be done by an expert. In 1 case the radiograph was said to show the foreign body in a bronchus, and tracheotomy and bronchoscopy followed at once, but no trace of the foreign body could be found. Another radiograph showed the foreign body in the cecum. It had evidently been in the esophagus when first seen. The foreign body is liable to induce spasmodic contraction which renders dangerous any attempt at instrumental exploration. In 2 cases the patients succumbed to sepsis from perforation of the esophagus by the instrument used in the attempts at extraction, remote from the actual site of the foreign body. V. Uchermann (Jour. Amer. Med. Assoc., from Norsk Mag. f. Lægevidenskaben, Dec., 1910).

Small bodies that pass into the stomach seldom give rise to trouble, being usually passed *per anum* a day or two later. In one of my cases, a child 3 years of age, the foreign body was a screw one and a half inches in length. It was passed on the third day without having caused the least discomfort. Large bodies, especially if sharp and hard, may, however, awaken dangerous complications.

> Case of foreign body in the esophagus in which the damage was done probably as the physician pushed down into the stomach a small piece of bone which had lodged in the upper part of the esophagus of a healthy woman of 53. She succumbed to the complications of the consecutive inflammatory process. In 3 other cases in the same clinic (Payr) 2 of the patients were saved by opening the thorax and esophagus. The other succumbed to sepsis. Only 9 are known to have survived in the 15 cases the writer has found on record of operative treatment of the phlegmon following the perforation. Jarasz (Med. Klinik, Aug. 4, 1912).

Treatment.—It is important to bear in mind, in all such cases, that a scratch or erosion of the mucous membrane produced by a passing angular bone—a fishbone, a pin, etc.—gives rise to symptoms simulating the actual presence of such a body. It is quite difficult at times to convince the patient that there is nothing in his gullet.

Cases in which dyspnea is a symptom demand immediate assistance. I have found this to be afforded most promptly by passing the index and middle fingers of the right hand into the mouth (which makes it possible to reach farther down than when one finger is introduced) and inserting the *middle* finger into the *left* pyriform sinus. The middle finger is then passed rapidly behind the larynx. The portion of the foreign body in the esophagus is thus reached and generally swept aside, drawing out of the larynx the part engaged in it or holding down the epiglottis. If it is impacted, the index finger is brought into use, and by closing upon the middle finger a grasp is obtained upon the obstructing substance. In some cases the larynx is deep-seated and is reached with difficulty, but the mouth of the patient can stand considerable stretching, if need be, considering the imminent danger of death. This procedure is, of course, only applicable in cases in which the foreign body is situated in the upper part of the esophagus and close to the larynx, but, as already stated, these alone expose the patient to immediate death.

When dyspnea is not present, the laryngeal mirror often greatly assists in the examination of the cavities involved, and it is rare, with a good light, that a body situated not far below the larynx cannot be detected. It also assists in properly introducing and directing any instrument or forceps that may be introduced. Round and smooth articles may be pushed down with a probang when they cannot be extracted with forceps. The horsehair probang, Graefe's coin-catcher, etc, are useful, but they must be used with gentleness. Emetics should never be used, since the contractions of the esophageal muscles tend to force the body through the walls of the organ.

When fishbones, meat, or meat-bones are impacted, **vinegar** hastens their disintegration and small quantities may be sipped. Foreign bodies that have passed into the stomach are said to be assisted in their migration through the intestinal tract by the use of **mashed potatoes** as food, but this, of course, will depend upon the nature and shape of the foreign body ingested.

Unless a competent esophagoscopist is at hand, the **bristle bougie** is the best device for removing foreign bodies, such as pins or fishbones, from the esophagus. A foreign body, if not too large or rough, may be pushed down into the stomach. When coins or similarly shaped bodies have lodged in the esophagus, if their position can be ascertained by means of the esophageal bougie or a skiagraph, either the bent esophageal forceps or an eight- to twelve- inch hemostat may often be successfully employed in their removal, even when the esophagoscope has failed to locate the offending object. The distance from the teeth to the object is measured, the instrument passed to its vicinity, opened anteroposteriorly, pushed gently for about an inch, and closed, and in most cases it will grasp or enclose the offending body. Unless the esophagus is inflamed it is not very sensitive, and so anesthesia is unnecessary unless the patient is nervous. If thought necessary, **cocaine** from 10 to 20 per cent., in a 1:4000 to 2:4000 solution, may suffice. In children over 4 or 5 years, excitable adults, or spasm of the esophagus, ether is indicated. To pass the esophagoscope the patient should be placed on the back with his shoulders from four to six inches beyond the end of the table, the head bent backward and supported by an assistant. The mouth-gag is used and pressure on the trachea avoided. The essentials for successful passing of the esophagoscope are that at first the head be bent backward, so as to straighten the cervical curvature and bring the axis of the oral cavity parallel with that of the esophagus, but as soon as the mouth of the esophagus has been passed the head must be brought slightly forward so that the instrument is directed downward and backward at an angle of about ten degrees. Ingalls (Amer. Jour. of Surg., Jan., 1912).

Irregular large bodies, tooth-plates, large bones, etc., when inaccessibly located, demand **esophagotomy** (*vide supra*) or **gastrotomy** (see STOMACH, SURGERY OF).

Tracheotomy is liable to give better results in the hands of the general practitioner than tedious attempts at extraction by the natural route, with the inevitable injury from them and the bleeding. If extraction is not promptly successful, an operation should follow without delay. In 11 cases reported the outcome was favorable in 9, recovery taking place in from two to seven weeks. One child who had swallowed a coin succumbed to pneumonia a week after the esophagotomy. The other fatality was in the case of a man of 41 who had swallowed two false teeth set on a plate. After attempts at extraction with fingers and induced vomiting had failed, a physician tried to push the set down into the stomach and apparently succeeded. H. Marschik and R. Vogel (Wiener klin. Woch., Oct. 14, 1909).

Esophagotomy is the modern method of treating cases of perforation of the esophagus by foreign bodies. The case reported is a sad commentary upon the frequent failure of ordinary attempts at removal in such instances. The foreign body consisted of a small piece of bone which the patient, a woman 53 years old, stated that she had been able at first to feel with the finger in the upper throat. A physician called three days afterward was said to have pushed down the bone with the stomach-tube, and in this way probably caused so much damage to the esophageal wall as to lead to a severe infection and inflammation. When admitted to the hospital she was in a marked septic condition, with a phlegmonous process in the neck and mediastinum. Operation was at once resorted to, the mediastinum being opened on both sides and an abscess about the esophagus exposed and evacuated. This was followed by esophagotomy and introduction of a tube to permit of feeding. Convalescence was rapid, the wounds healing except on the right side, where discharge of a purulent secretion persisted. On the twenty-ninth day, when the patient was no longer in the hospital, a profuse hemorrhage took place from the wound in the neck on the right side, which necessitated ligature of the right common carotid. The woman recuperated, but nine days later developed a cerebral abscess and basal meningitis, with fatal termination. The cerebral abscess and meningitis were probably due to infectious emboli. From this experience and others the writer cautions urgently against the forcing down of foreign bodies into the stomach and the customary methods of extraction without the aid of the eye. T. Jurasz (Intern. Jour. of Surg., from Med. Klinik, Nu. 31, 1912).

INJURIES OF THE ESOPHAGUS.

The esophagus is often involved in injuries inflicted with suicidal intent, the ingestion of corrosive fluids and attempts at throat-cutting being the chief casualties of this kind met with in practice. Many accidents occur also through the accidental swallowing of acids or strong alkalies,—concentrated lye, for instance,—or a household disinfectant, such as carbolic acid, or, again, boiling tea or coffee from the spout of a vessel. A corrosive substance taken by a suicide is usually taken hastily and thrown, as it were, far back into the mouth. Spasm of the larynx usually ensues and collapse follows. The same effect is generally, however, produced in accidental cases, and the lips, the gums, or even the front part of the tongue do not always indicate the severity of the lesions produced. If death does not immediately occur from laryngeal spasm,—*i.e.*, asphyxia and shock,—severe pain is experienced and acute esophagitis (see below) ensues. Wounds of this region due to accidents or military weapons are extremely rare, however, but one injury of the esophagus, for instance, having been recorded during the Rebellion. The protected position of the esophagus anteriorly and posteriorly seems to account for this, the sternum and spinal column acting as shields.

ESOPHAGITIS.

Symptoms.—In cases arising from injury of the esophageal tissues pain is marked, especially during deglutition, unless the traumatism be of such a nature as to completely destroy the tissues and their nervous supply, as sometimes happens when caustic acids are swallowed. Under these circumstances slight pain in the periphery of the disorganized mass is the general result. The pain usually experienced is continuous and dull, and usually follows the long axis of the sternum, extending to the back and neck. Motions of the head or shoulders sometimes aggravate it. At times it is burning, especially if the lesion is not deep-seated and when regurgitation of the acid gastric contents occurs. Spasm is frequent in such cases. A sensation suggesting the presence of a foreign body is complained of.

After a lapse of time, varying with the gravity of the injury, hematemesis may occur, owing to the contraction of the muscular supply around the ulcerated areas that are undergoing the process of repair; but this is generally of short duration. Large quantities of mucus and mucopus are often voided.

The sequelæ of these cases are usually serious. Even after slight injuries, sometimes, cicatricial stenosis occurs that leads to esophageal stricture.

The presence of blood in the food and localized pain suggest that a foreign body may be present when no other clear indication is furnished by the history. This form often becomes phlegmonous and is usually attended by a febrile reaction. Pseudomembrane may also be vomited: indicative of the form of stenosis present. Thrush, it must be remembered, may be attended by no other symptom than impediment to the passage of food.

In some cases the local inflammatory symptoms—difficult deglutition, the mucopurulent discharge, etc.—continue for some time. Such cases are termed *chronic* esophagitis by some authors.

Diagnosis.—In traumatic cases the history and the symptoms render the diagnosis easy. The location of the pain usually points to the seat of the lesion; this may be verified by the passage of the esophageal sound: a dangerous procedure in severe injuries. In acute esophagitis occurring in the course of febrile diseases a condition with which it may be confounded is the irritation following repeated vomiting of acid substances. The discomfort resulting from this, however, is of short duration, while the symptoms of true esophagitis are continuous and more marked.

Etiology.—Almost all cases of acute esophagitis are due to mechanical and chemical irritation or destruction by caustic acids, hot liquids, and foreign bodies. Cases due to the ingestion of acids are often met in connection with attempts at suicide, while the two latter exciting factors usually come into play accidentally. Carbolic acid is most frequently used by suicides, while the accidental agents are boiling liquids, concentrated lye, and spicules of bone.

Acute inflammation also occurs as a complication of infectious fevers, typhoid fever, typhus, pneumonia, pyemia, small-pox, etc., while pseudomembranous esophagitis may be caused by extension of a disease, such as diphtheria, in which a false membrane is present. Various pharyngeal disorders complicated with abscess may also extend to and involve the esophagus in the inflammatory process. Malignant neoplasms, especially carcinoma, of the esophagus may be accompanied by acute esophagitis. Among the rare causes are: the prolonged administration of tartar emetic (Laennec), vertebral abscess, laryngeal perichondritis, and hysteria.

It is occasionally met with in sucklings without explainable cause.

Pathology.—Desquamation of the epithelium and erosions are present when comparatively mild caustics or strong solutions of them have been swallowed, but, when such agents as pure carbolic acid, concentrated lye, etc., have been taken, the entire mucous lining may be deprived of its epithelium. It then becomes greatly swelled, and purulent infiltration usually follows the primary serous infiltration. The mucous layer may thus be detached from the underlying tissues. Foreign bodies may also cause deep-seated lesions and be surrounded by a cushion-like mass, causing temporary esophageal stenosis. Gangrene occasionally follows, necrotic masses being ejected, generally with vomitus. The local disorder occurring as complication of fevers, etc., is usually less marked, though diffuse purulent inflammation occasionally occurs.

Treatment.—The treatment must necessarily be symptomatic since the inflammation is but the expression of local repair, though we may influence this process so as to avoid stenosis as after-effect. When one is fortunate enough to discover the cause at once, local measures may prove useful. If the lesion is due to some mineral acid, **lime water** should be used; if to caustic alkalis, **vinegar** is indicated. **Iced fluids** and, if the patient can swallow, **white of egg** are particularly useful in all cases due to corrosion. An **ice-bag around the neck** often subdues the pain.

Feeding, when possible, should be limited to cold, soft, bland substances, preferably milk, soft-boiled eggs, or hard-boiled egg-yolk reduced to flour and mixed with the milk. If deglutition is difficult, the upper portion of the esophagus—which is usually the seat of severest lesion—and the pyriform sinuses (on each side of the larynx) can be slightly anesthetized with a spray of 4 per cent. solution of **cocaine,** applied with a curved-tip atomizer so as to localize it. Or, **orthoform** may be insufflated with a powder-blower in the same region; besides producing analgesia, this agent acts as an antiseptic. An injection of **morphine,** one-half hour before meals, also reduces markedly the local hypersensitiveness during deglutition.

All these various measures are also indicated to relieve the continuous pain. Small pieces of **ice** allowed to melt slowly in the mouth afford comfort by causing constriction of the engorged vessels; and **ice-cream** is a very agreeable article of food which produces the same effect. In some cases the patient must be fed *per rectum* until disappearance of the acute phenomena.

Chronic esophagitis may occur as a result of the acute form, but in most instances it is due to passive engorgement of the veins owing to obstruction of the circulation through disease of some organ, the liver in cirrhosis, the kidneys in Bright's disease, etc. The engorgement may be such as to cause rupture of one of the esophageal veins and fatal hemorrhage occur therefrom. Most cases occur in alcoholics.

The treatment resolves itself into measures calculated to overcome the causative disorder. A milk or very low **diet** is indicated when the varicose state of the esophagus is marked, alcohol, coffee, tea, and other agents capable of raising the blood-pressure being strictly avoided. Agents which reduce the blood-pressure are useful to deplete the engorged vessels. The following mixture, which also contains a local sedative and astringent, may be used:—

℞ *Potassii bromidi*	ʒij (8 Gm.).
Tincturæ veratri	ʒj (4 Gm.).
Bismuthi subnitratis .	ʒiiss (10 Gm.).
Mucilaginis acaciæ ..	℥iss (46 Gm.).
Aquæ cinnamomi q. s. ad	℥iv (124 Gm.).

M. Sig.: Shake well before using, and sip 1 tablespoonful on retiring.

During the day the effect may be kept up by means of the following:—

℞ *Acidi tannici*	gr. j (0.06 Gm.).
Cocainæ hydrochlor..	gr. ⅙ (0.01 Gm.).
Extracti glycyrrhizæ.	gr. ij (0.13 Gm.).
Sacch. alb.	gr. j (0.06 Gm.).

M. et ft. trochiscum no. j.

Sig.: Allow 1 to dissolve slowly in the mouth four times daily, between meals.

STRICTURE OF THE ESOPHAGUS.

Symptoms.—Narrowing of the esophageal lumen—whether due to cicatricial contraction or to tumors, intramural or extramural; aneurisms, etc.—is attended by gradually increasing difficulty in swallowing, referable, in the majority of instances, to a particular spot under the sternum. At first solid food is passed with increasing difficulty, and the patient finds it necessary to masticate with great care or swallow smaller boluses. A feeling of pressure is usually experienced as the food gravitates downward, which in some cases enables the patient to gauge the steadily decreasing rapidity with which the food reaches the stomach. Later on these masses require the assistance of fluids, and finally only the latter can pass with ease.

In 1 of 2 cases of obstruction of the esophagus witnessed by the writer, the first is of interest as showing the length of time a large, irregular-shaped, foreign body can be retained in the esophagus. The patient, a man aged 34, had swallowed his upper false teeth during sleep, temporarily causing obstruction to swallowing. For nine weeks after that he suffered no pain except during the act of swallowing, which caused him some distress. Neither he nor his physician had located the foreign body in the esophagus, but it was shown by a skiagram. The shape of the body rendered its removal by direct traction inadvisable, on account of the danger of injury to the esophagus and of possible cellulitis; it was therefore removed by an open operation at the side of the neck, which is described. Convalescence was uneventful. The second case is of interest as a hitherto undescribed type of esophageal obstruction and a peculiar swallowing symptom which it presented—substernal distress on swallowing acid substances. This had lasted for five years. The first theory was that the patient had an aneurism of the arch of the aorta, but the X-ray showed a calcification stiffening the vessel and causing pressure on the esophagus by the upper part of the base of the heart, the two causing a slight delay in transit in this portion of the tube. When the food or drink was acid it irritated the mucous membrane and caused the symptom described, which subsided when the food had passed into the stomach. A. Bassler (Jour. Amer. Med. Assoc., March 15, 1913).

The first effort at swallowing at a meal is generally the most arduous, the subsequent boluses passing with comparative ease. Various motions of the head are resorted to by the patient in the vain hope to assist the act of deglutition. As the difficulty increases, the patient gradually becomes weakened and emaciated through deficient nutrition.

Greater attention should be paid to the neurasthenia underlying the dilatation of the esophagus in most cases. Of his 6 cases, all but 1 were men between 24 and 56. Symptomatic treatment is necessary, repeated on recurrence of trouble. It is thus possible to keep the patients free from disturbances for many months at a time, even when a complete cure is not possible. The spasm of the cardia responsible for the trouble generally comes on suddenly; the frequent remissions of longer or shorter duration are characteristic, as also the alternation with spastic phenomena elsewhere and the impossibility of introducing the sound beyond the cardia at times, while at other times it slips smoothly in. Jüngerich (Med. Klinik, Aug. 27, 1911).

In stricture due to cancer the contraction is rapid and death from pneumonia is not uncommon. When this does not occur, the tissues around the esophagus are gradually implicated by extension, and death occurs from marasmus due to general toxemia, this being greatly encouraged by starvation. The sense of hunger, however, is not acute. The vomited materials are often tinged with blood, and the general facies of the patient soon serve to indicate the presence of a malignant neoplasm. Glandular infiltration occurs late in the disease.

Three cases of benign cryptogenic stricture of the esophagus which have occurred in the writer's practice within a year. All were in the cervical part of the esophagus and the patients were women. One was 32 and the others each 67 years of age. In 1 there was also a pocket which was opened. When an elderly or middle-aged patient complains of difficulty in swallowing it is usually apt to be diagnosed offhand as due to nervousness or cancer, according to the length of time it has existed. Ocular inspection through the esophagoscope is the only means of obtaining a positive diagnosis, and in these cases the nature of the condition could not have been ascertained any other way. All the patients recovered perfect capacity for swallowing. W. Lerche (Jour. Amer. Med. Assoc., April 19, 1913).

Diagnosis.—Certain points serve to locate the seat of the stricture. Regurgitation of the food usually occurs immediately when the stricture is situated near the upper orifice. That the rejected food has not reached the stomach can easily be recognized by the absence of the characteristic odor. The material ejected is also alkaline instead of strongly acid: a valuable diagnostic feature. When the narrowing is low down the esophagus is dilated above, and the food is accumulated in the pouch-like cavity formed. Regurgitation, instead of occurring promptly after the ingestion of food, only takes place several hours later, and is mixed with considerable mucus. Here, again, the material ejected is not acid, having failed to reach the stomach. The accumulated food sometimes causes dyspnea by pressing upon the trachea.

The X-ray method aided by bismuth to afford an outline of the esophageal canal permits an early recognition of the stricture. Esophagoscopy is, of course, of great value in this connection.

> Stricture of the esophagus as a result of increased mediastinal pressure is not an uncommon occurrence and is rightfully looked upon as an important sign of mediastinal disease. Such a pressure upon the esophagus may be exerted by enlarged mediastinal glands, malignant disease of the mediastinum, aortic aneurism, mediastinal or spinal abscess, pericardial effusion, chronic adhesive mediastinitis, etc. Clinically such pressure is recognized in two ways; the patient complains of dysphagia and the stomach-tube or esophageal bougie meets with resistance at the site of compression. By the introduction of the bismuth X-ray method in the examination of the esophagus it has been shown that the stomach-tube or bougie will not register the very earliest encroachment upon the lumen of the esophagus, but will show only those constrictions that are of considerable degree. Lange (Med. Rec., Jan. 16, 1909).
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> Esophagoscopy is comparatively easy in children, as the mouth of the esophagus is not closed, as in adults, but gapes rhythmically with inspiration. In cicatricial stenosis the writer introduces a narrow **bougie** with the aid of the esophagoscope and leaves this bougie in place for a few hours. This prepares the way for sounds of a larger caliber, and it is thus possible to stretch the lumen to normal size in time in most cases. If not, circular **electrolysis** through the esophagoscope renders invaluable service. He has had 54 patients with cicatricial stenosis resisting all ordinary measures. Only 10 required **gastrostomy**; all the others were cured by the above measures through the natural passages; 21 of the patients were children and all but 2 were cured. Guisez (Bull. de la Soc. de Pediatrie, June, 1911).

Auscultation of the esophagus may sometimes be employed with advantage; provided, however, the examination be conducted in a very quiet room. The stethoscope is usually employed, but direct application of the ear along the left of the spine—while the patient brings his shoulders as close together anteriorly as possible—is far more satisfactory. A peculiar, irregular, wave-like bruit is heard when liquid is swallowed, followed by a second splashing sound as the fluid reaches the stomach. When a stricture is present the wave-bruit and the splashing sound are varied in proportion, the latter being absent in some cases of advanced constriction or replaced by repeated splashes following one another more or less in rapid succession.

Far more precise, however, is the information acquired by means of the esophageal sound—especially the graded, olive-tipped, flexible bougie. The patient being placed upon an ordinary chair (avoiding one with a high back), the physician stands behind him. He should use his left hand as guide for the instrument, by placing it on the patient's face so as to bring the index and middle fingers over and parallel with the patient's mouth. The patient's head being thrown back, the bougie (warmed and lubricated with glycerin) should first be passed between the fingers and then introduced into the mouth perpendicularly—much as a sword-swallower introduces the weapon. The olive-tip, however, should *not* penetrate the esophageal canal by passing *over* the larynx, but into the pyriform sinus on either side of the larynx. Each sinus affords a funnel-like aperture which allows the bougie to glide easily into the esophagus, without encountering the bodies of the cervical vertebra or the cricoid cartilage. The instrument should not be forced down, but allowed to drop into the cavity by reason of its own weight. The present method of introducing the instrument over the middle portion of the pharyngeal wall, and therefore over the center of the epiglottis and the posterior surface of the larynx, is defective, and accounts for the resistance usually encountered while introducing the instrument.

Frequently a spasm of the muscles causes the instrument suddenly to be arrested; but after a few seconds this ceases and arrest only occurs at the seat of the stricture. When this happens the instrument should be allowed to remain *in situ;* after a few moments it often suddenly drops lower down. In some cases it is advisable to first anesthetize the pharynx and that portion of the esophagus within reach with a 4 per cent. solution of cocaine. When permanent arrest occurs below the larynx, the spot (gauged by length of bougie introduced) should be estimated and a slightly smaller bougie then tried. This is repeated until one is obtained that penetrates the opening—of which it affords an approximate diameter for future comparison. In some cases only narrow catgut will pass. Gum-elastic stomach-tubes may be used, but they do not afford the exact information obtained from the olive bougie. It should not be used, however, when an aneurism is known to cause the stricture.

Great care and gentleness should invariably prevail. The procedure is not devoid of danger even in the hands of an expert, softening of the tissues, especially in the low strictures, readily yielding to the pressure of the instrument. I have witnessed a case in which a pint of milk was thus introduced into the mediastinum, as shown by the autopsy.

The presence of stricture having been determined, the history almost invariably points to its original cause. The case should be *completely* examined, however; a history of syphilis with tertiary pharyngeal symptoms may be obtained, for instance, and the stricture be ascribed to cicatricial stenosis, while in reality the true cause may be an aneurism. All the etiological factors should be borne in mind and the prevailing one determined by elimination.

In stricture due to cancer the stenosis is usually situated where the left bronchus forms a ridge in the esophageal mucous membrane, but no portion of the canal can be said to be exempt. The vomited matter is often tinged with blood and the cancerous facies soon serves to establish the diagnosis. Emaciation is generally very rapid. The possibility that a stricture may be cancerous imposes additional care in the use of the bougie, the friability of the cancerous tissues being such as to easily yield to even slight pressure. A stricture occurring after the fortieth year in a man whose history does not present strong evidence of syphilis, tuberculosis, or local injuy is usually cancerous.

Etiology.—Stricture of the esophagus may be congenital, but it occurs, in the majority of cases, as a result of lesions produced by the ingestion of corrosive liquids.

> The frequency in children in Austro-Hungary of corrosion of the esophagus from drinking lye is shocking. At the Stefanie hospital at Budapest there have been in the last nine years 516 cases of acute disturbances from this cause, and 267 cases of cicatricial stenosis of the esophagus, all the result of leaving a solution of lye, ready to be used in washing, within reach of young children.
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> The writer has found it possible to examine the condition with the Roentgen rays by having the children swallow a soft porridge containing 30 or 40 per cent. of oxide of zirconium. This substance is insoluble in acids, strong alkalies, etc., and seems to have no action when injected subcutaneously into animals, so that no toxic action need be feared from it; for Roentgen work it has several advantages over bismuth. As the child swallows each mouthful of the porridge, the progress of the mouthful down the gullet can be watched with the Roentgen rays, and the regions where it passes along smoothly and where it seems to be arrested or makes its way slowly are marked and compared. By this means it has proved possible to detect multiple strictures. Flesch and Peteri (Jahrbuch f. Kinderheilkunde, June, 1911).

Ulceration occurring as complication of infectious diseases, particularly typhoid fever. Syphilitic ulceration of the esophagus, though, is usually followed by stricture varying in degree with the location of the ulceration and the area involved. Impacted foreign bodies, masses of thrush-fungus, local tuberculosis, injuries—*i.e.*, all conditions capable of causing severe acute esophagitis—may act as primary causes. A greatly enlarged thyroid, an aneurism, an intramural abscess, enlarged lymphatic glands, growths of the mediastinum, etc., may also, by pressure upon the esophagus, reduce its lumen. Cancer of the esophagus may act as cause.

A comparatively frequent cause of stricture is squamous epithelioma: almost the only form of neoplasm encountered in the esophagus. It is usually met with in men, and after the fortieth year.

Pathology. — The pathology of stricture varies with the cause, but in practically all cases due to local lesions, excepting cancer, the prevailing feature is the presence of cicatricial tissue. In cases originating from the ingestion of corrosive fluids the stricture is usually high, spasm of the esophagus generally preventing gravitation of the liquid to the lower part of the organ. In all others, even syphilis, the chances are that the stricture—there is generally but one —will not be far from the lower third, or lower down. The extent of tissue involved varies frequently, and occasionally the whole lumen of the esophagus is more or less involved and distorted. In the majority of cases in which the stricture is low, there is sacculation or dilatation of the portion above the stenosis.

Prognosis.—In case of cicatricial stenosis the prognosis is quite favorable under appropriate treatment. Without treatment the contraction usually reduces the lumen sufficiently to prevent alimentation, and the patient dies of slow starvation. Cases due to cancer are naturally hopeless, while the prognosis of cases resulting from the pressure of surrounding growths, aneurisms, etc., depends upon the degree of curability of the latter.

Treatment.—The aim of the treatment is obviously to restore the lumen of the esophagus to its normal dimensions as nearly as possible, but in cancerous stricture this is hardly indicated, the neoplasm itself involving complications that bring on a fatal issue. For this reason a distinct line should be drawn between cases of stricture due to cicatricial lesions—*i.e.*, injuries, syphilis, tuberculosis, etc.—and those due to a malignant neoplasm. In all of the former **dilatation with** the **bougie** may be said to be required as soon as a stricture has been recognized; in cancerous stricture the procedure should not be resorted to. It but inflicts severe suffering upon the patient and involves additional risk.

> The writer commends the regular passage of **bougies** as affording much comfort to the patient and enabling him to take a much larger variety of food with ease. An oval or Mackenzie bougie is best; the author has had a modification of this instrument made which, by tapering to a point, facilitates its entrance and passage through the stricture. The largest size of bougie than can pass should be used, and when passed it should be kept in position at least ten minutes. The procedure should be repeated every other day, using a larger size of bougie if possible on each occasion. When the stenosis has been overcome by the passage of the largest bougie, further regular treatment may cease, but a bougie should be passed at intervals to prevent recurrence.
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> Where the stenosis is increased by spasm, much help is obtained by the use of the bromides in addition. **Thiosinamine** was used by the author in several cases of cicatricial stenosis in conjunction with the bougies, being given hypodermically twice a week for some weeks in each case. While sometimes it did not appear to have any appreciable effect, in 6 cases it was decidedly helpful and in 1 gave, in combination with the bougies, a most satisfactory result.
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> Where cicatrices are of syphilitic origin, thorough **mercurial inunctions** are necessary.
>
> **Excision** of a simple **stricture** situated close to the upper end of the gullet should be attempted only where the obstruction is extreme, and will only be successful where the stricture is of very limited extent. Excision of a cicatricial stricture at the cardiac orifice has been successfully performed by means of a preliminary **gastrostomy.** Where an obstruction is so severe as to interfere with the nutrition of the body, the operation of **gastrostomy** must be thought of. Walker Downie (Glasgow Med. Jour., June, 1912).

Cicatricial stricture may be expected in all serious injuries of the esophagus. Hence, after an accident or a local disorder known to be followed by cicatrization, stenosis should be prevented by dilatation with bougies employed in the manner indicated under DIAGNOSIS. **Dilatation** should be begun as soon as there is a reasonable evidence that an ulcerative process no longer exists, and be repeated daily, beginning with a medium-sized tube and ending with one representing the normal diameter of the esophagus. The surgeon should not wait until symptoms of stenosis appear, since this often occurs only after considerable narrowing of the lumen. In some cases stenosis returns as soon as the bougies are not introduced, and the patient is required to personally use the instrument during the rest of his life. Whether begun early in the history of the case or late, the procedure is generally effective, but in old cases the tissues yield with difficulty and sometimes greatly tax the patience of surgeon and patient. It is sometimes necessary to begin with catgut, which can be left *in situ* until the following visit, when the smallest bougie can often be introduced. The catgut does not prevent the passage of liquids and the patient can be fed as usual. As large a bougie as the stricture will admit is then introduced every day, and a larger one substituted every few days until the largest number is easily passed and retained several hours daily.

> In simple cases dilatation with **bougies** is used, preferably slow, from a few hours up to twenty-four hours. Complex cases require visual search to find the lumen (endoscope), which is usually lateral. **Dilatation** is instituted. Brünings has devised special probes for this internal **esophagotomy,** either with esophagotome, a Guise guide, or with hidden blade. Electrolysis has not been tried by the writer. In cases requiring external surgery, **gastrotomy** is used as a preliminary; this allows the use of probes and permits keeping them in place from twenty-four to forty-eight hours, feeding being through the new gastric mouth, and dilatation of the esophagus may be in either direction. Sargnon (Arch. intern. de laryn. d'otol. et de rhin., Sept. and Oct., 1912).

Permanent tubage of the esophagus, introduced by Symonds, of London, has won much favor. The tubes are "from 4 to 6 inches in length and are made of gum-elastic upon a silk web, the outside and inside being as smooth as possible. The upper end is funnel-shaped so as to rest upon the face of the stricture, and slightly flattened on one side (that it may not press unduly against the back of the cricoid) and the margin is perforated in two places for the attachment of a silk thread. The other end is hollow, with a lateral opening. The tube can be introduced upon a bougie, but it is more easily managed with a proper whalebone guide set in a suitable handle. The exact site of the stricture is ascertained first and marked upon the guide; the greatest gentleness must be used, and as soon as the point enters the narrowest part the tube is slowly pushed onward until the resistance to the funnel is felt; the guide is then withdrawn and the silk thread attached to the tube tied around the ear or fastened with strapping. A tube of this kind can be left for two or three months without being changed, the patient swallowing liquid food through it. As a rule, however, it is necessary to remove the first after three or four days, as the stricture always dilates to some extent, and sometimes this must be repeated. Even if it should slip through, it will pass *per anum* or remain lodged in the stomach without inconvenience" (Mansell-Moullin). This method is said to be devoid of risk to life, and a sufficient amount of food can readily be ingested.

When these short tubes cannot be used or when they cause cough during deglutition Krishaber's or Morell Mackenzie's long tubes, or, better still, a long, catheter-like rubber tube can be employed and left *in situ* several days at a time.

> In stenosis of the lower end of the esophagus, it is important to have the proper kind of bougie. The only reliable instrument is a long 24- or 25-inch whalebone **bougie,** stiff enough so that it will not bend, but will go straight through where it is directed. A second point is the use of the silk thread swallowed the day before so as to allow it to become firmly engaged in the bowel below the stomach. This is a simple but highly commendable procedure, owing to the fact that it enables the operator to introduce the bougie or dilator directly to the permeable point of the stricture and to use such force as is required to pass on into the stomach with a certain knowledge that his instrument is not going to deviate to the right or left and perhaps make false passage into the lung or pleural cavity. H. L. Akin (Western Med. Rev., Feb., 1911).

Operative procedures are sometimes resorted to.

Internal esophagotomy, an operation based on that of urethrotomy, wherein the cicatricial bands are cut, has not given the satisfactory results claimed for it. It is only warranted in cases of annular stricture. **Esophagostomy** is preferred when the stricture is high enough to be reached through the side of the neck, the incision being made between the pharynx and larynx on the left side, toward which the esophagus leans in this region. The trachea then finds itself on one side of the incision and the carotid sheath on the other. The location of the stenosis having been determined, it is as nearly as possible made to correspond with the upper part of the incision, which should also include the esophagus. Sometimes the omohyoid must also be incised. A rubber tube is then introduced, and the permanent fistula formed serves for its easy introduction and withdrawal. The patient can thus be easily fed, the tube passing under the stenosis. The operation is not an easy one, owing to the proximity of large vessels and other easily wounded structures.

In cancerous stricture it is inadvisable to pass **bougies,** as already stated; but a soft-rubber **catheter** with large fenestra, passed every other day or oftener, often serves to keep the passage open. It may also be left *in situ* and serve for the introduction of liquid food. **Rectal feeding** should be resorted to when esophageal alimentation becomes impossible, but when rectal feeding in turn becomes insufficient — which often happens when continued several weeks — **gastrotomy** should be resorted to. Through the opening thus obtained to the interior of the stomach it is possible to very satisfactorily supply the patient with all the food he requires. The improvement is usually rapid, and comparative comfort is insured until the toxic effects of the neoplasm bring on death.

> The history of the case and examination with simple instruments soon clears up the diagnosis, but little can be done in treatment. A **gastrostomy** affords but temporary relief, although this spares the cancer the irritation from passage of food and thus has a marked palliative influence in addition to its permitting feeding. But the general toxic action of the malignant disease is not checked and it is seldom possible to keep the patient alive for more than two or three years. The retention cannula suspended in the stricture has not given good results; gangrene from pressure is liable, and the growth of the tumor pushes the tube up out of the stricture. The same

objections apply to Senator's and Schreiber's dilators. Better results were obtained with the cautious use of ordinary **sounds.** Local application of radium has not given good results. When emaciation begins systematically the writer advises an operation rather than to let the patient drift away with nothing done, and thus gives him a longer lease of life. Ewald (Med. Klinik, Dec. 15, 1912).

DILATATION OF THE ESOPHAGUS.

Etiology and Symptoms.—Dilatation of the esophagus may be congenital, as stated, but in the majority of cases it occurs as the result of stenosis of the lower end of the tube, which, by its resistance to the passage of food, causes its accumulation in the esophageal canal. To compensate for this the walls become greatly hypertrophied. This condition is followed, as elsewhere, by softening, which in turn causes the canal to yield to the pressure of its contents, and to become greatly enlarged.

Generally, small quantities of food are passed into the stomach at a time, and the pouch-like cavity becomes gradually emptied between meals. But regurgitation occurs when this process is too slowly performed, and the frequent invasion of the larynx by the food thus brought up causes strangling and cough, besides the dysphagia experienced.

In nearly every case of idiopathic dilatation there is a spastic stricture at the cardia, either primary or secondary, and all trouble subsides as a rule when this stricture is conquered. Sedatives internally to control the stricture never benefited in his experience, nor galvanization, and recurrence followed generally in the cases in which Hacker's method was applied. Permanent recovery was obtained by Mikulicz in 5 out of 6 cases in which he **forcibly stretched** the **cardia** with forceps introduced through an opening into the stomach, and others have obtained equally favorable results with this measure and Reisinger from **resection of the dilated portion.** Temporary relief can be obtained by repeatedly **rinsing out** the **dilated esophagus.** Mintz (Arch. für Verdauungskrankheiten, Aug., 1911).

Meltzer's swallowing sound is helpful, when detected, in identifying the case as one of dilatation.

Both cardiospasm and idiopathic dilatation of the esophagus are present if Meltzer's swallowing sound is clearly heard either immediately or seven seconds after deglutition. Cardiospasm is frequently present if it is considerably delayed from twelve to twenty seconds after swallowing water, or if it is now delayed, and now absent. There is, as a rule, idiopathic dilatation of the esophagus if the sign is always absent, and bougies (43° to 48° F.) enter the stomach. Radiographs will confirm the diagnosis, and are valuable as aids. Max Einhorn (Med. Record, March 1, 1913).

The bougie may be used to advantage, the large dimensions of the cavity and the narrow orifice met below being characteristic. Side-pouches may cause the sound to be arrested if it is not introduced perpendicularly or if distention of the canal is present.

Typical example of the "pulsion" diverticulum and of diffuse dilatation in the upper and lower parts of the esophagus. In the one case the father of the patient had a similar affection, confirming the congenital tendency to special weakness of the muscle at the junction of the pharynx and esophagus. The physiological internal pressure in the esophagus, to propel the food along, causes protrusion of this part of the wall, with formation of a diverticulum in time, As it is due to the propulsion of the food, it is called a "pulsion" diverticulum. The disturbance in swallowing, regurgitation, tumor in the neck and murmur suggested the diagnosis, which was confirmed by Roentgen-ray examination. F. Umber (Arch für Verdauungskrankheiten, Feb., 1910).

Treatment is futile unless any stricture present be itself reduced, either by the **sound** or by **surgical removal of the constricted area.**

When strictures can be completely eradicated, the esophagus tends to resume its normal caliber, but it is aided by **galvanism,** the positive pole being passed into the esophagus and the negative externally, preferably between the shoulder-blades.

A dilated esophagus allows remnants of food, layers of mucus, etc., to attach themselves to its walls and to accumulate in the fundus of the pouch formed. The latter should be washed out daily with warm water through a stomach-tube. If the lower stricture is narrow, much of the fluid containing the offending substances is returned. After each meal the patient should perform exercises consisting in compression of the chest after deep inspirations to force food into the stomach.

The cardinal feature from the start is to **nourish** the patient. Fluids, milk, cream, soft-boiled eggs, and other semifluid foods can be ingested, when taken in small quantities and at intervals, pass, though slowly, until the stricture is too narrow even for small sounds. Swallowed with the usual speed, even such food accumulates, and is regurgitated, causing sometimes dangerous strangling. If food no longer passes alone, a Symonds tube can be used, or rectal feeding resorted to, pending surgical removal of the strictures.

Insufflations of finely powdered **tannin** and **bismuth,** equal parts, are sometimes helpful after **washing out** the **esophagus,** to promote contraction.

Analysis of 91 cases of diffuse dilatation of the esophagus treated by **dilating the cardia** with the hydrostatic dilator, no anatomical stenosis having been detected. Four of the patients died since treatment, the known causes being pneumonia, tuberculosis, and rupture of the esophagus, the cause being unknown in 1 case; 73 were completely relieved from their dysphagia and 11 were not. The cures have lasted from one to six or seven years. A few at long intervals are still conscious of the food passing the cardia. In the writer's earlier work the degree of pressure varied with the tolerance of the patient, but he does not now consider this a safe guide. The patient whose esophagus was ruptured did not complain of pain till after the dilator was withdrawn. The pressure of 675 mm. has invariably given marked relief and in the majority a complete cure. The routine practice has been to give two or three treatments and then let the patients return home, telling them to return if the dysphagia recurs. It is remarkable that most patients with extreme inanition have needed but one treatment for a cure. In no case has it been given at frequent intervals for any length of time. H. S. Plummer (Jour. Amer. Med. Assoc., June 29, 1912).

CARCINOMA OF THE ESOPHAGUS.—This form of tumor is relatively rare in the esophagus, Walshe, for example, having found but 13 cases out of 8298 deaths from carcinoma. This does not include, however, cancer of the cardic end of the stomach, which is usually considered as cancer of the latter organ.

The esophagus appears to be invaded but rarely by cancerous growth, for, out of a series of 722 cancers in all parts of the body only 6 were found in the esophagus. It seems to enjoy a certain degree of immunity from neoplasmic invasion in contrast with the organs lower in the alimentary tract. Zenker and von Ziemssen have collected reports of 5079 autopsies, of which 0.36 per cent. showed esophageal cancer and 0.25 per cent. were primary. W. T. Cummins (N. Y. Med. Jour., Feb. 15, 1908).

Symptoms.—Cancer of the esophagus is attended with progressive stenosis, as already stated under the head of STRICTURE OF THE ESOPHAGUS. In some cases, however, the facies of the patient and cachectic symptoms denoting the involvement of other organs are first to appear. Pain is marked early in the cases; later on the tissue destruction involves the nervous supply, and the pain is no longer experienced. Slight hemorrhages may occur at this stage, though streaks of blood may have already been noted in the vomited matter. The cancerous process is then apt to invade the surrounding organs,—the larynx, the trachea, the bronchi and the lung, the pleura, the pericardium, and the larger vessels,—causing fatal hemorrhage. The cervical glands are often enlarged. The vertebræ may be included in the destructive process and involvement of the cord, with paralytic symptoms, appear. Paralysis of the larynx may also occur through pressure on the recurrent laryngeal. Progressive emaciation begins early in the history of the case and death from exhaustion finally supervenes.

In 78 of the 104 cases of cancer of the esophagus reported, progressive difficulty in swallowing was the first sign of trouble. There was no pain in 61 cases, but in 5 cases pain preceded the dysphagia by a few days and in 11 cases they came on together. In 29 cases there was no pain until a month or two after the difficulty in swallowing had developed. In 19 of the 40 cases with pain it occurred only while food was being swallowed; in the others it was continuous. Regurgitation was the rule; it was absent in only 17 of the total 104 cases. The appetite remained good in 70 per cent. and there was distaste for meat in only 4 cases. The cancer proved fatal in most cases between six and twelve months, but in a few, in from two to four months. In 7 cases the inability to swallow the food came on suddenly, the patients being apparently in perfect health; 1 was a man of 32. In 2 of these cases intense pain accompanied the sudden dysphagia, which in 1 case was accompanied by profuse salivation. In 8 cases the sudden difficulty in swallowing proved permanent and no solid food could be swallowed thereafter; in 2 other cases neither solids nor fluids could be swallowed.

Cancer is differentiated from spasm of the esophagus by the rapid sequence of the disturbances, gastrostomy becoming necessary in from one to four months, while spasm of the esophagus may persist for years without requiring this. Copious salivation and mucous vomiting are aids in diagnosing. In 1 case a woman of 28 had an evident spasm of the esophagus, but its persistence, notwithstanding great fluctuations, indicated an underlying organic lesion, confirmed by direct visual inspection and death five months after the first symptoms.

In 6 of the cases, the cancer did not prove fatal for from one to two and one-half years; 12 of the patients developed tuberculosis. L. Lanny (Jour. Amer. Med. Assoc., from Arch. des mal. de l'app. digestif, Aug., 1910).

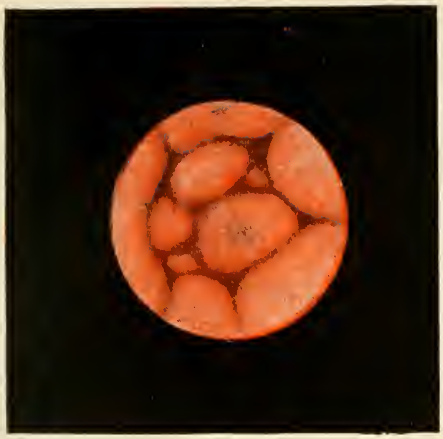

Fig. 1.

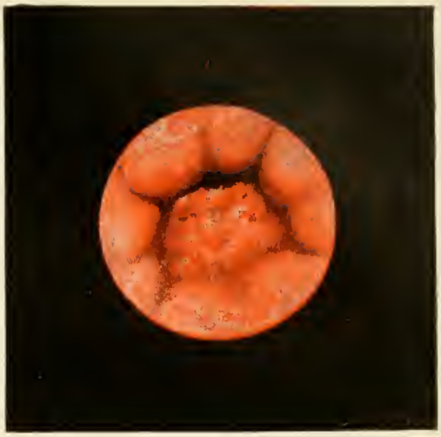

Fig. 2.

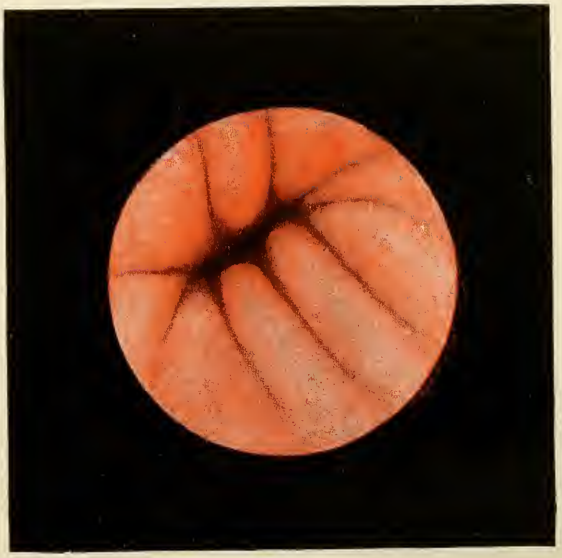

Fig. 5.

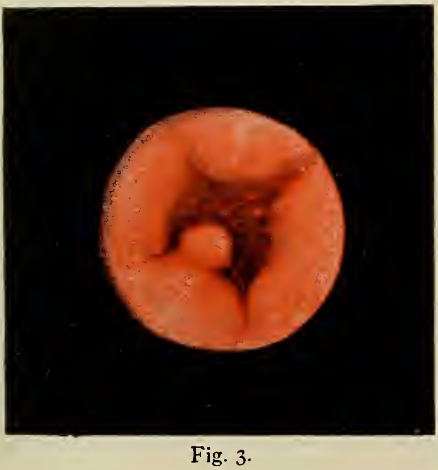

Fig. 3.

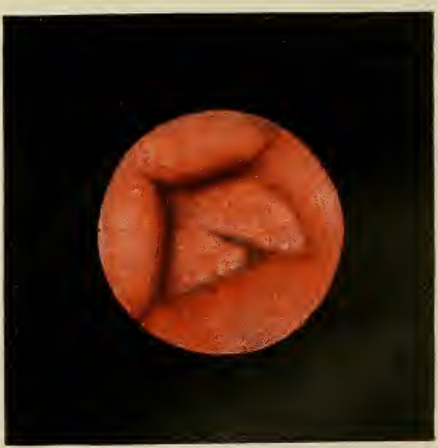

Fig. 4.

Esophagoscopy and Gastroscopy in Cancer of the Esophagus and Stomach.
(*H. H. Janeway* and *N. W. Green.*)

Fig. 1, epithelioma in lower third of esophagus. Fig. 2, cardiac carcinoma seen through the partially dilated cardiac sphincter. Fig. 3, carcinoma of cardiac portion of the stomach. Fig. 4, carcinoma some distance within stomach. Fig. 5, entrance to the pyloric region of stomach as viewed through an indirect telescope inserted three to four inches within stomach.

Surgery, Gynecology and Obstetrics, September, 1911.

[illegible]

[illegible]

Diagnosis.—Progressive stenosis is a feature of all cases of stricture; hence the diagnosis must be based upon other symptoms. When the facies of the patient, a family history of cancer, and absence of local injury, syphilis, or tuberculosis can be recorded in a patient aged over 40 years, the likelihood that cancer is present is very great. Ejecta of portions of the mass will then reveal the characteristic histological features of cancer.

> In cancer of the upper third of the esophagus the author has found what he terms progressive retrofixation of the tongue to be a very early and characteristic sign. The tongue cannot be protruded by the patient more than a few centimeters without his feeling pain, and when the examiner exerts traction on the organ an unusual degree of resistance is noticed. This sign was not observed in cases of functional spasm, tuberculosis, or syphilis of the esophagus, even at an advanced stage of the disease. It is probably due (1) to a periesophagitis attending the cancerous process, which binds the esophagus to the trachea in front and the prevertebral fascia behind; (2) to fixation of the esophageal mucous membrane to the outer layers constituting the wall of the organ, thus preventing free motion of the lingual mucous membrane, with which it is connected, and (3) to changes in the hyoglossus, chondroglossus, and stylohyoid muscles. Guarnaccia (Archiv. intern. de laryn., d'otol., etc., July-Aug., 1912).

In the majority of cases, however, such clear signs cannot be obtained. Then pressure from a growth external to the esophagus must be excluded; an aneurism, an enlarged gland, etc., may, as shown, cause stricture. If the stenosis is near the larynx it is rarely cancer, but a cicatricial stricture or an impacted foreign body. The auscultation test described may be employed and also the esophageal bougie, but the latter must be used with extreme care. (See STRICTURE.)

Cancer of the esophagus can usually be readily diagnosed by the history and by sounding, but it is much more difficult to diagnose cancer of the cardia in an early stage. Esophagoscopy is, therefore, scarcely of secondary importance for cancer of the esophagus, but it is extremely valuable in cancer of the cardia. The annexed colored plate clearly illustrates the diagnostic value of these measures.

Etiology and Pathology.—Almost all cases of cancer encountered in the esophagus are of the squamous-epithelioma variety, the growth starting from the pavement epithelium of the mucous membrane, most frequently in that of the lower third of the organ. It gradually invades the mucous membrane, and, progressing laterally, the lumen of the cavity is soon reduced by a ring-like neoplasm. Later, the deep tissues become involved and the epithelioma, if the patient lives long enough, may extend to any of the important organs of the thoracic cavity.

Cancer occurs especially in males over 40 years of age. An inherited predisposition and an exciting cause —such as the prolonged use of alcohol, strong condiments, or an ulcer— are thought to afford the necessary conditions for its development.

Treatment.—If located at the junctions of the pharynx or stomach, **surgical removal** may prolong life.

> Aboral end of the esophagus and the cardiac portion of the stomach must be considered as one surgical

region. Cancer in this location is by no means infrequently met with. It permits of an early diagnosis by means of the gastroscope. An operation of practical utility for resection of cardiac cancer must remove not only a portion of the esophagus, but also a considerable part of the stomach, in particular the lesser curvature. It can be accomplished without undue tension by an end to end anastomosis with suture. It has rendered possible for the writers to obtain operative recoveries out of 17 dogs and 5 out of the last 6. It may be stated that the death of the recovered animals about six weeks after the operation was due to an interference with the normal physiology of the pylorus, and may be prevented by simple pyloroplasty. From a technical standpoint such an operation can easily be performed upon the human being. By this method the authors have operated upon a patient with cancer of the cardiac portion of the stomach involving the esophagus. The patient had had symptoms for the preceding nine months, and the operation required was an unusually severe one. The spleen was involved in the carcinomatous mass and was removed in one piece, together with the stomach and lower portion of the esophagus. The patient died fifty-four hours after operation, of empyema, starting, apparently, in a small perforation situated in the circle of anastomosis, a complication which can be more carefully guarded against in the future.

This clinical experience, however, and the condition of the specimen removed demonstrate that the technique employed was satisfactory and that the operation is feasible and justifiable. Janeway and Green (Annals of Surg., July, 1910).

Cancer of the esophagus offers an ideal situation for the treatment by **radium**, particularly as it extends so slowly by means of glandular infection.

When the disease affects a portion of the esophagus in the neck, it is possible to **remove the growth** in its entirety and yet leave the patient in a condition of comparative comfort after the operation. The operation is to excise the portion of the esophagus affected by cancer, together with any glands, keeping well away from the diseased area, and to replace the segment of esophagus removed by means of a strip of skin cut transversely from the neck and retaining an attachment and blood-supply, the continuity of the esophagus being completely restored. After an interval of sufficient length for the firm union of the skin esophagus to the portion of the normal esophagus at the lines of section, the attachment of the flap of skin by its base to the skin of the neck is divided, and any lateral aperture in the skin esophagus which may remain is closed. Except when the growth involves the extreme upper limit of the esophagus or invades the upper aperture of the larynx, it would probably be possible to avoid performing tracheotomy. Till the edges of the skin esophagus have united to those of the esophagus, a tube for feeding purposes should be retained in position. Lane (Brit. Med. Jour., Jan. 7, 1911).

An opening should be made into the stomach before the operation and the patient fed through this for as long a time as possible to exclude risk of infection of the field of operation. Winiwarter (Wiener klin. Woch., April 4, 1912).

Feeding by the mouth can be carried on for some time through the esophageal tube, but the insertion of the latter becomes increasingly dangerous, especially if any force is used, as ulceration increases, since it may find its way through the diseased area, and direct the food into the pleura or mediastinum, with prompt fatal result. **Rectal feeding** should therefore be begun early, especially when signs of ulceration are present.

Report of 26 cases of cancer of the **esophagus, especially in the early stages, treated by direct application of radium.** In 3 incipient cases this treatment caused a disappearance of the dysphagia and obstruction by the tumor, with formation of cicatricial tissues, while in 23 of the more advanced cases it acted as a palliative, reducing the difficulty in swallowing. The application of radium was made by enclosing 0.01 to 0.02 Gm. (⅙ to ⅓ grain) and later 0.05 to 0.1 Gm. (¾ to 1½ grains) in a capsule suspended by silver wire and introduced by means of an esophageal sound. Its insertion was followed by abundant salivation, which was regarded as due to the action of the radium, since it failed to result from the insertion of the sound itself. The applications were repeated at intervals of two days, the total duration of the treatment being sixty hours. The most favorable results were obtained in the smooth, infiltrated type of esophageal cancer without marked proliferations or ulcers. Guisez (Inter. Jour. of Surg., from Gaz. des hôp., No. 58, 1912).

The **diet** should be regulated according to the stage the cancer has reached. When ordinary food can no longer be swallowed, meat finely scraped, hashes, soft rolls, besides the usual semiliquid foods, such as mashed potatoes and milk, rice pudding, etc., should be given as long as possible to sustain strength. When even hashed or scraped meat cannot be endured, eggs may be used in increased quantities, raw or soft-boiled, to compensate for them. Then the diet should be exclusively liquid or semiliquid, using the catheter—very carefully introduced—if need be. A feeding instrument described by Delavan many years ago is very useful. It can be made with an ordinary soda-water bottle. Rectal feeding should be resorted to when all these measures fail to nourish the patient adequately. The mouth-washes are very useful in these cases and should be used frequently, and solution of **cocaine** gradually increased from 4 to 10 per cent. in strength, if needed, used with the atomizer before each meal to prevent pain during deglutition. **Morphine** should be used freely in these cases when they become hopeless, or if surgical procedures offer no reasonable chances of recovery.

The dysphagia is greatly aided by the use of the following pastils, according to Thomas:—

℞ *Cocaine hydrochloride*	0.0025 Gm. (1/25 gr.).
Morphine hydrochloride	0.005 Gm. (1/12 gr.).
Antipyrin	0.10 Gm. (1½ gr.).
Sugar	0.30 Gm. (5 gr.).

One or two of these pastils should be taken before each meal.

As an alterative prescription the following is recommended:—

℞ *Dionine hydrochloride,* *Codeine hydrochloride* .....of each	0.10 Gm. (1½ gr.).
Cocaine hydrochloride	0.25 Gm. (4 gr.).
Ammonium valerianate, *Bitter-almond water,* of each	7.50 Gm. (2 dr.).

Of this solution, 15 drops should be taken three or four times a day.

When the descent of food is hindered in cancer of the esophagus, Liebermeister recommends that the patient sip small amounts of **hydrogen peroxide** solution of 1 to 2 per cent. strength. A cleansing of the cancerous surface occurs which is sufficient to allow of easy passage of the food. Even in cases where rectal feeding has been found necessary this plan will often succeed. The peroxide solution should be sipped at intervals of an hour.

The value of **hydrogen dioxide** in this affection, recently pointed out by Liebermeister, is confirmed by the writer. Liebermeister showed by X-ray and pathological studies that absolute stenosis, anatomically speaking, is never present in cancer of the esophagus or cardia. There is almost always a channel permitting the passage of fluids, no matter what the degree of stenosis. Complete obstruction of this channel only occurs when it is occluded by food material not sufficiently divided before swallowing and by the products of decomposition of the necrotic tumor-mass. In these cases 1 dessertspoonful of 1 to 3 per cent. hydrogen peroxide solution is given every hour. In less than twenty-four hours the stenosis is overcome and in a few days the patients, who had previously been completely unable to swallow anything, can eat purées and even solid food. The distressing subjective symptoms simultaneously disappear. The patients may even gain in weight and recuperate so much as to present a normal appearance. One of Liebermeister's patients gained 8½ kilos (18 pounds). The author refers to a case in which 5½ kilos were gained in four weeks. The patient then left the hospital, still taking the peroxide; but later he neglected its use for several weeks, with the result that he was obliged to return to the hospital. Upon resumption of the treatment for two weeks, 6 kilos were gained. The same cycle of events was then repeated, the beneficial effect of the measure being thereby clearly shown. In scirrhous cancers the peroxide produces little or no effect, but in the other types it constitutes one of the best palliative measures now available. S. Fradiss (Progrès méd., July 27, 1912)..

There should be given orally only such food as will readily pass through the stenosis. The treatment with **hydrogen dioxide** is to be maintained for weeks and months. When the stenosis is absolute the patients are to receive nourishment by rectum and only the hydrogen dioxide solution by mouth for two or three days; the administration of fluid food may then be begun and will be found possible in most cases. If even then no fluid will pass through the stenosis, the patient receives subcutaneously 0.01 Gm. ($\frac{1}{6}$ grain) of **morphine,** or 0.001 ($\frac{1}{60}$ grain) of **atropine,** or half of this dose in combination, half an hour before the time for meals, three times a day for several days. The introduction of sounds should be considered a last resource, of which use should be made only in exceptional cases.

NEUROSES.

Spasm of the Esophagus (Esophagismus). — *Symptoms.* — Spasmodic contraction of the muscles of the esophagus comes on suddenly, several attacks occurring in quick succession or intermitently, efforts to suppress them by swallowing saliva or food usually bringing them on. Deep-seated, cramp-like pain is experienced during the spasm in the majority of cases. Food on its way down to the esophagus may be regurgitated if still near the larynx; if below this it is retained *in situ,* until the spasm has passed. The attacks may last but a few hours and recur only after months' intervals; again, they may be persistent and render proper alimentation of the patient impossible without recourse to auxiliary means. Solids can, as a rule, be swallowed.

True spasm as the result of organic disease of the nervous system is considered a rare condition; whereas functional spasm is of frequent occurrence and sometimes responsible for secondary lesions of a gross nature. Hill (Jour. laryn., rhin., and otol., Feb., 1912).

Diagnosis.—The constriction usually occurs near one of the extremities of the esophagus, but it may not be limited to these regions in succeeding attacks. Hysteria and other neuroses can usually be detected, especially in females, for whom the disease shows a predilection. The bougie may be used advantageously to distinguish esophagismus from the organic lesions already described. In spasm the instrument will encounter a stenosis during the active stage and pass down freely while no spasm is present.

Etiology.—Spasm of the esophagus is the manifestation of a general neurosis, particularly hysteria, and is therefore observed in young females. It may occur as a symptom of tetanus, rabies, epilepsy, chorea, and other neuroses, and as a result of violent emotions,—fright, joy, etc. It may also be associated reflexly with pregnancy, and with disorders of the genital system, or of other organs, especially the neighboring ones,—the pharynx and the stomach. It often attends the various organic diseases of the organ itself.

Treatment.—Treatment should be directed to the symptoms. The painful deglutition, inability to swallow solids, and the choking sensation are usually promptly relieved by the passage of the **esophageal sound,** the moral effect adding its share to the good result. Sometimes, however, this procedure increases the spasms. Inhalations of **nitrite of amyl,** by relaxing all vessels, diminishes the volume of blood supplied to esophageal muscles, and, therefore, their tendency to spasm. The **bromides,** or rectal injections of **chloral,** 15 grains (1 Gm.), in free solution, can be used for a similar purpose. In some cases the spasms are kept up by nasopharyngeal catarrh and cease when this condition is properly treated. Antispasmodics, such as **camphor** and the valerianates, especially the **zinc valerate,** are sometimes useful. An **emetic** sometimes proves efficacious, especially when, as sometimes occurs, the cause of the spasms, a foreign body, is brought up. A **cocaine spray,** using a 5 per cent. solution, before meals, is useful to facilitate the ingestion of food and its retention. In some hysterical cases **suggestion** will alone prove useful. The patient, for instance, may be suspended by the arms to a crossbeam and kept there some time, with the verbal assurance that on being freed her spasms will cease.

Paralysis of the Esophagus. — Symptoms.—Paralysis of the esophagus is rarely met with. There is functional inactivity of the muscular coat of the esophagus and great difficulty is experienced in swallowing, the bolus remaining *in situ* if at all large. Liquids pass down with ease and are used by the patients to "wash down" small masses of solid food. The accumulation of food in the esophagus often engenders dilatation, and the symptoms of the latter disorder are the predominating ones.

Etiology.—Paralysis of the esophagus is usually due to extensive bulbar paralysis and other central nervous disorders. But it may also occur in a complication of peripheral disorders, especially diphtheria, enlarged lymphatic glands, and of syphilis, alcoholism, plumbism, etc.

Treatment.—The treatment indicated is that of the causative disorder. In diphtheric paralysis **arsenic** is most effective. After a course of this remedy hypodermic injections of strychnine are often effective. **Faradism,** the negative pole in the sulcus diectly in front of the sternomastoid and the positive back of the neck, may be simultaneously employed.

C. E. de M. Sajous,
Philadelphia.

ETHER (sulphuric ether). — C. W. Long, in 1842, was the first to employ ether as an anesthetic in surgical operations, though to C. T. Jackson, a chemist, and W. G. T. Morton, a dentist of Boston, belongs the credit of securing for it general recognition (1846).

Ether ($H_3C.H_2C.O.CH_2.CH_3$ or $(C_2H_5)_2O$; specific gravity, 0.716 to 0.717 at 77° F.) is chemically diethyl oxide and is obtained by the gradual addition of 90 per cent. alcohol to heated (140° C.) concentrated sulphuric acid, which combines with a portion of the alcohol present to form ethyl hydrogen sulphate ($C_2H_5.H.SO_4$); the latter, in turn, reacts with the remaining alcohol to form ether, which is distilled off and then purified by shaking with water and an alkali, and redistillation.

Ether appears as a colorless, mobile liquid, having a characteristic, penetrating odor, generally regarded as pleasant, and a sharp, burning taste. It is much more soluble in water than is chloroform—1 in 10 or 12 instead of 1 in 200—and mixes in all ratios with alcohol, chloroform, benzene and fixed and volatile oils. Pure ether will take up water to the extent of 1 part of the latter in 35 parts of ether.

It is very volatile, evaporating more rapidly than chloroform at ordinary temperatures, and has a much lower boiling point—96° F. (35.5° C.). instead of 140° F. (60° C.) in the case of chloroform. Ether vapor is heavier than air, and since it is very inflammable, its use for anesthetic purposes in the presence of artificial light other than incandescent electric bulbs is attended with danger, unless the light be placed at a considerable distance above the patient. A mixture of ether vapor and air, when ignited, explodes violently.

Ether is officially permitted to include about 4 per cent. of alcohol, the latter containing, in turn, a little water. The alcohol has been generally considered to act as a preservative for ether, but more recently this has been shown to be an error. The presence of alcohol in ether is of no value except where the anesthetic is given by the drop method, when the alcohol obviates excessively rapid volatilization of the ether and consequent chilling of the apparatus employed (Baskerville).

Impurities in ether may depend either upon the use of unsuitable alcohol in its production—*e.g.,* ethyl alcohol denatured by methyl alcohol, when the product obtained will be an ethyl ether mixed with methyl or methyl-ethyl ether ("methylated ether"), or upon the addition of impure ethyl alcohol to a pure ether for the doubtful purpose of rendering it more suitable for anesthetic use, or, again, upon the formation of adventitious substances, partly owing to improper storage of the originally satisfactory ether. Prolonged exposure of ether to light and air may result in the production, during anesthesia, of such symptoms as coughing and suffocation, as well as serious after-effects.

> The presence of excess moisture in ether should be guarded against, since contact with water, or moist air, in time gives rise to various objectionable impurities. Oxidation of ether in the presence of moisture is productive of a series of complex conversions, initiated by the formation of hydrogen dioxide. Ether of anesthetic grade contains peroxidized compounds after exposure to varying temperature conditions and sunlight, in the presence of atmospheric oxygen, for considerable periods, especially when stored in colorless glass vessels or in badly stoppered tin containers.
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> Acetaldehyde, the presence of which may account for some of the observations made in practice, is one of the impurities most likely to be generated by exposing partially filled containers to varying atmospheric conditions. Practically all ethyl alcohol contains some acetaldehyde. Ether should not be stored in glass vessels for any length of time without being tested for oxidation products before use. Tin containers should be of such capacity that they need not be opened without being emptied when the ether is employed for anesthetic purposes.
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> Ether for anesthesia should always be tested for acidity, peroxides and aldehyde, and the presence of the last should be rigorously guarded against; or the ether, if so contaminated, should be administered by a method which eliminates these impurities before it is introduced into the system. Baskerville (Jour. Amer. Med. Assoc., Nov. 23, 1912).

Aldehyde in ether may be detected by occasionally shaking 10 c.c. of ether in a test-tube, during one hour, with 1 c.c. of a 6 per cent. solution of potassium hydroxide in water. Neither of the liquids should show any coloration at the end of the hour; otherwise aldehyde is present (U. S. P.). Undue acidity of ether may be tested for by dipping blue litmus paper, moistened with water, into ether for ten minutes. No residue or foreign odor should be left when ether is allowed to volatilize from an evaporating dish or from odorless blotting paper.

> Ether for anesthesia should not be affected by a solution of potassium iodide, for six hours; should not change or discolor pieces of potassium hydrate, for six hours; and when shaken with Nessler's reagent, should produce a milk-white turbidity without a yellowish-brown, dark-gray, or black precipitate. Kamensky (Roussky Vratch, June 16, 1912).

PREPARATIONS AND DOSES.—In addition to its uses as an anesthetic, ether is frequently administered internally. Its official preparations are as follows:—

Æther (ether), required to contain about 96 per cent., by weight, of absolute ether. Dose, 10 to 60 minims (0.6 to 4 c.c.).

Spiritus ætheris (spirit of ether), composed of 32.5 parts by volume of ether and 67.5 parts of alcohol. Dose, ½ to 2 fluidrams (2 to 8 c.c.).

Spiritus ætheris compositus (compound spirit of ether; Hoffmann's anodyne), consisting of 32.5 parts by volume of ether, 2.5 parts of ethereal oil ("heavy oil of wine," consisting of several ethyl esters and other substances, and imparting to the preparation a special "bouquet"), and 65 parts of alcohol. Dose, ½ to 2 fluidrams (2 to 8 c.c.).

[The B. P. recognizes two sorts of ether: (1) Æther, only required to contain 92 per cent. by volume of pure ether, and (2) Æther purificatus, or ether freed from most of the alcohol and water, and having a specific gravity of 0.720.]

PHYSIOLOGICAL ACTION.—Rapid absorption of ether takes place in the lungs when its vapor is inhaled, as it is possessed of a high vapor tension and penetrates the tissues with great facility. All mucous membranes absorb it promptly, and the same physiological effects may be secured—though more slowly—by its ingestion as by the customary route of administration. Locally, it causes temporarily a pronounced irritation of the sensory nerve-endings and vessel-walls, followed by a dulling of sensibility. It is less irritating, volume for volume, however, than chloroform, though in practice this difference is more than counterbalanced by the fact that a much larger amount has to be introduced than of chloroform to produce an equal general anesthetic effect.

> Preliminary excitation from anesthetics is probably a universal effect, as deduced from their action on protoplasmic streaming in vegetable cells. Positive chemotaxis has also been observed as the effect of ether upon certain bacteria. Ether likewise hastens the development of flowers. Blumfeld (Practitioner, Sept., 1907).

That ether, like chloroform, is capable, in sufficient concentration, of paralyzing the life processes in any form of cell is illustrated in that it arrests the streaming of the protoplasm in plant cells, as well as the activity of the cilia in the ciliated epithelia of animals. If its action be soon discontinued, recovery of function occurs; but where it is kept up for a certain minimal period, cellular death takes place. Thus under the prolonged direct influence of ether the irritability of nerve-tissue is permanently lost, rigidity of muscle-tissue supervenes, and the red blood-cells are destroyed.

Rapid evaporation of ether is accompanied by a sudden and marked absorption of heat, which is easily capable of inducing a fall in temperature in adjacent bodies to below the freezing point. This is the chief factor in the production of local anesthesia with ether, though direct paralysis of the terminal nerve-filaments and endings by the anesthetic itself may also play a part.

Nervous System.—The characteristic general anesthetic action of ether is due, according to the Meyer-Overton theory, to its dissolution in the lipoids or complex fatty substances of the nerve-cells, the function of which is thereby temporarily interrupted, through loss of the normal relationships of the lipoids to the remaining cell-constituents. The reason for its accumulation in these—and other—fats is that it is more soluble in these fats than in the water of the blood itself. In the beginning of anesthesia, at least, the blood returning to the right heart from the general circulation contains less ether than that entering the left heart from the pulmonary circulation, for the anesthetic has been taken up from the blood by the various fatty tissues it has reached in its systemic journey. At no time, however, does the blood completely give up its ether to the fats; the condition present at the height of anesthesia is one in which the ratio of the ether present in the blood and fats corresponds with the relative solubilities of ether in these two different media. Rises and falls in the ether content of the blood are soon paralleled by proportionate rises and falls in the nervous tissues. Once a sufficient degree of anesthesia is attained, the amount of ether to be supplied is approximately only that which will maintain a sufficient percentage of the gas in the air-cells to balance that in the blood and prevent any of the ether in the blood from being re-excreted. The depth of anesthesia in any given period depends not only upon the amount of ether that has already been introduced into the organism and reached the nerve-tissues, but upon the percentage of ether in the inspired air. As soon as the air-ether mixture is diluted to a certain degree, ether begins to pass out from the blood and the percentage of ether in the expired becomes greater than it is in the inspired air.

Experiments with animals have constantly demonstrated that the anesthesia can be shortened or suspended altogether if a suspension of lecithin is injected intravenously soon after the animal has come under the influence of the anesthetic. Nerking (Münch. med. Woch., Aug. 18, 1908).

Ether differs from chloroform in that its effect appears more slowly, in the greater concentration of vapor required to bring about anesthesia, and in the greater margin of safety, *i.e.,* the greater difference between the concentration of vapor which will just bring on anesthesia and that which will cause death. Thus, Nicloux showed in dogs that whereas, in deep chloroform anesthesia, the percentage of the anesthetic in the blood averaged 0.05 per cent., that of ether under the same conditions was 0.13 to 0.14 per cent. Again, whereas Rosenfeld showed in rabbits that a 3.5 per cent. ether vapor is required to bring on complete anesthesia by inhalation and a 6 per cent. ether vapor must be used to cause respiratory arrest, Spenzer found that the corresponding figures in the case of chloroform are approximately 1.0 and 1.6 per cent. At least 3 times as great a percentage of ether as of chloroform in the inspired air is required for anesthesia (Gottlieb).

The action of ether on the nervous system is similar to that of chloroform and of large amounts of alcohol, consisting in a progressive paralysis of various brain centers, sometimes preceded by a short stage of stimulation.

Report of researches on the action of anesthetics on the nervous system in frogs. The order of susceptibility of different portions is: (1) sensory centers of the cortex; (2) motor centers of the same; (3) spinal cord; (4) bulb; (5) sensory nerve-fibers; (6) motor nerve-fibers; (7) muscle. Joteyko and Stefanowska (Progrès méd., Oct. 19, 1901).

In a timid, nervous individual with perhaps some organic heart lesion, ether has a distinctly stimulating effect. Ingle (Amer. Jour. of Surg., July, 1911).

A circumstance sometimes overlooked is that even before consciousness and tactile sensation have been completely lost, analgesia may be present. In deeper anesthesia, the centers of consciousness and other brain centers become entirely paralyzed, and finally the spinal cord is involved, the reflexes disappearing and the muscles finally completely losing their tonicity. The functions of the respiratory and vasomotor centers, however, are not endangered until a still larger quantity of the drug has been introduced, and the art of anesthesia consists in avoiding encroachment of the effects of the drug on these centers, while maintaining the action on the receptive and motor nuclei.

Circulation.—The heart rate is always increased in ether anesthesia, often to 90 or 100 per minute. This effect is due, at least in large part, to direct or reflex actions on the extracardiac governing centers of the heart, since it is wanting if the nerves to the heart have been cut. There has been produced no evidence to the effect that ether directly stimulates the heart muscle (Gottlieb), though the vasoconstrictor action of ether, by increasing the blood-pressure, may result in a better supply of blood to the heart.

The peripheral vessels of the skin, especially in the face, are dilated by ether. This effect is different from that of chloroform in that it persists during the anesthesia, the skin remaining flushed throughout, whereas with chloroform the flush tends to give way gradually to pallor. The splanchnic or internal vessels, on the other hand, are constricted by ether, probably owing to an action both on the vasomotor center and the vessel themselves. This vasoconstriction more than offsets the simultaneous peripheral vasodilatation, and in conjunction with the increased heart rate causes an increase in the blood-pressure, which generally persists throughout the anesthesia, when the latter is not prolonged. Such a rise in pressure, more or less marked, is an almost constant accompaniment of ether anesthesia. The effect of chloroform differs in that there is a tendency to direct depression of the heart and splanchnic vessels, and the blood-pressure gradually falls during anesthesia. In perfusion experiments chloroform has shown itself to be about 35 times as depressing to the heart muscle as ether. Only after prolonged deep ether anesthesia does the heart become depressed and the splanchnic circulation relaxed.

Reflex fatal cardiac inhibition, through irritation of the trigeminal terminals in the upper respiratory passages and transmission of the impulse to the vagi, is far less likely to occur with ether than with chloroform: (1) because the direct depressing action of the drug on the heart is far less than in the case of chloroform, the cardiodepressing action of which strongly predisposes to inhibition of the heart, and (2) because of the wider latitude in the concentration of the vapor administered in the case of ether.

Respiration.—Ether tends to stimulate the respiratory center, probably both directly and through excitation of the afferent vagal nerve-paths from the lungs. The breathing is at first accelerated and deepened. In the stage of excitement it becomes irregular. In the narcotic stage, however, it is regular again and slightly slowed, afferent impulses no longer exciting it owing to the general sensory paralysis.

Where the ether is pushed beyond the stage of anesthesia proper, the respiratory movements may gradually dwindle in their amplitude until arrest occurs, or they may come to a standstill more or less suddenly. Respiratory paralysis by ether usually occurs at a time when the heart is still capable of maintaining a good circulation, and recovery is usually readily secured by artificial respiration. With chloroform, on the other hand, the heart is already considerably depressed when the breathing ceases and artificial respiration is not as effectual as under ether.

Blood. — Like chloroform, ether, when circulating in the blood, is present in greater concentration in the red blood-cells than in the plasma, owing to the lipoids present in the former. In high concentration it readily produces hemolysis. In the course of ordinary ether anesthesia, a slight, temporary decrease of the hemoglobin in the blood has been shown to take place.

> Ether causes blood destruction; those who believe otherwise are misled by the concentration of blood due to preliminary treatment and sweating during the administration. The color index almost always (49 out of 50 cases) falls and the number of corpuscles increases, showing marked blood destruction and increased production of corpuscles deficient in hemoglobin. Sections of marrow of the femur of a rabbit etherized to death showed marked erythroblastic proliferation. The hemoglobin is absolutely reduced after etherization, as shown by reduction in individual corpuscular hemoglobin value. The increased hemolysis which occurs is nature's effort quickly to replace the destroyed corpuscles, and the regenerated cells are lacking in hemoglobin.
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> It is urged that whenever possible one or two blood examinations be made before preparation of the patient for etherization. Less than 50 per cent. of hemoglobin indicates that an anesthetic is dangerous and only allowable in vital emergencies. J. Chalmers Da Costa and J. L. Kalteyer (Boston Med. and Surg. Jour., June 13, 1901).
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> The viscosity of the blood is increased by deep and lessened during light narcosis. These differences cannot be considered of great importance. The changes in the specific gravity pursue a parallel course to those in the viscosity in the case of light ether narcosis, while during narcosis with chloroform the inverse relationship exists. R. Burton (Jour. of Physiol., July 13, 1905).
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> A series of experimental observations on ether anesthesia showed that: (*a*) The hemoglobin is slightly reduced, causing a slight anemia. (*b*) Hemolysis is not materially increased. (*c*) The changes in hemoglobin and erythrocytes are explainable on the basis of blood inspissation. (*d*) Ether causes a marked decrease in the coagulation time, most marked from the seventh to the tenth days. Nitrous oxide causes no permanent effects of any significance; ether causes more harmful changes, while chloroform causes the most harmful results (hemolysis and production of distinct anemia). Hamburger and Ewing (Jour. Amer. Med. Assoc., Nov. 7, 1908).
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> Report of experiments made to determine the effects of ether on the phenomena of bacteriolysis, agglutination, and phagocytosis. The typhoid bacillus was used and the experiments were conducted *in vitro* by adding ether in varying amounts to both normal and immune typhoid serum, and also *in vivo* by observing the effect of ether anesthesia on these properties of the serums of practically normal individuals, normal rabbits, and rabbits immune to the typhoid bacillus. Ether was found to reduce markedly the phagocytosis of streptococci *in vitro,* and also, after an ordinary ether anesthesia, with streptococcus, pneumococcus, *Staphylococcus aureus, B. coli,* and *B. typhosus.* The reduction of the phagocytic powers of blood after an ordinary ether anesthesia in different experiments lasted from two days to several weeks and was due apparently to a direct effect on the leucocytes and serum without any action on the bacteria. A very small addition of lecithin *in vitro* restored the phagocytosis. E. A. Graham (Jour. Amer. Med. Assoc., March 26, 1910).

Temperature. — During anesthesia a gradual fall in temperature occurs, owing to the dilatation of the skin vessels, which accelerates heat loss, and muscular inactivity, which results in diminished heat production. The anesthetic is in addition believed to depress the heat centers. In advanced stages of narcosis, another factor favoring low body temperature is introduced when circulatory activity becomes impaired.

Chloroform produces a loss of body temperature approximately equal to that produced by ether. Surrounding the field of operation with wet towels will greatly increase the loss of body temperature and should therefore be studiously avoided. The loss of temperature produced by ether narcosis will not be greatly increased by the preliminary administration of a moderate dose of morphine. Warming the ether vapor before inhalation will prevent the loss of body temperature, or may actually increase it in a degree proportionate to the temperature of the vapor and also to that of the operating room. Patients should not only be kept dry and warm, but be anesthetized in a room free from draughts, and should not be transferred to a cold room, even after the anesthetic is discontinued. Davis (Bull. Johns Hopkins Hosp., April, 1909).

Metabolism.—Some metabolic processes are slowed during anesthesia, but on the next day there is observed an increased elimination of nitrogenous waste-products in the urine. The urea excretion, however, is subnormal, while ammonia and uric acid are increased; this shows that the products of cell metabolism have been only imperfectly broken down.

The conception regarding the nature of inhibition of oxygen metabolism in narcosis is of a purely hypothetic character. It is only an established fact that narcotics induce an acute asphyxia of the cells. Herein is the essence of narcosis. During sleep, restitution occurs. The irritability, which becomes reduced in the course of the day as a result of the fatiguing action of sensory stimuli, gradually rises again, principally by the action of oxygen. In narcosis there is, on the contrary, a depression of the oxidation processes. Experiments show that even with a free supply of oxygen a fatigued ganglion cell does not recover at all during narcosis. There occurs, rather, a gradual asphyxia, and, although this process is only developed to a small extent in light narcosis, still it presents just the reverse of that which sleep brings to the ganglion cells. M. Verworn (Bull. Johns Hopkins Hosp., April, 1912).

There also occurs an increase in the sugar content of the blood—hyperglycemia — and some interference with the metabolism of fats, acetone and diacetic acid being not infrequently found in the urine.

Elimination.—Ether is eliminated unchanged, chiefly by way of the lungs, and very slightly through the kidneys and skin. Its excretion is distinctly more rapid than that of chloroform, this accounting for the fact that recovery from anesthesia occurs more quickly where ether is used than with chloroform. According to the experimental work of Nicloux, the elimination of ether is as complete in two hours after the cessation of its administration as in seven hours after chloroform. The relative insolubility of chloroform in the water of the blood as compared with ether (approximately 1 in 200 instead of 1 in 10) causes it to remain more steadfastly in the fatty tissues in which it is freely soluble, with the result that the elimination of the last traces of anesthetic is effected more slowly than in the case of ether.

ETHER AS AN ANESTHETIC.—Ether possesses the following advantages over chloroform: Greater immediate safety; less likelihood of causing fatty degenerative changes in the parenchymatous organs; more rapid excretion of the drug. The first of these is the most important, and under most circumstances is of itself sufficient more than to offset numerous advantages of chloroform such as more rapid action, less likelihood of excitement during the induction of anesthesia, rarity of pulmonary complications, less flow of mucous secretions, etc.

> Ether should be used as an anesthetic in **obstetric practice** when pulmonary complications are absent. Its action upon the uterine contractions in the second stage of **labor** is preferable to that of chloroform. No anesthetic should be given in the first stage of normal labor. Uterine atony and post-partum hemorrhage are rare following ether anesthesia. Ether should be used in **eclampsia** in preference to chloroform. Its action is as positive and the danger much less. It is safer to the mother than chloroform. The danger of delayed poisoning is slight. H. M. Stowe (Surg., Gynec. and Obstet., Feb., 1910).

> The author always administers ether in **thyroid** cases and in **trephining operations,** and has not noted any undue congestion or hemorrhage, which has so often been charged against ether as an anesthetic in these cases, and which, no doubt, does apply to any method where the air is restricted. Samuel Johnston (Can. Pract. and News, March, 1912).

The comparative safety of ether as an anesthetic has been amply shown by statistics. Those of Foy, based upon 877,507 chloroform administrations, show a mortality of 1 in 4301 for this anesthetic, while those of Julliard, based upon 314,738 ether administrations, show a mortality of only 1 in 14,987. Hewitt, combining the figures of Julliard with those of Ormsby, and calculating from a total exceeding 1 million anesthesias, found a death rate of 1 in 3162 for chloroform and 1 in 16,302 for ether. The number of chloroform anesthesias has of late years shown a marked decrease in the United States.

> Report of 112 responses to question blanks sent out to surgeons concerning their anesthesias during 1908. Chloroform was used in 20,613 cases, with 1 death to 2060; ether in 11,859, with 1 death to 5930; chloroform plus ether in 10,232, with 1 death in 3410; and the scopolamine-morphine mixed anesthesia in 23,809 cases, with 1 death in 4762. Local anesthesia or the first whiffs of ether were utilized in fully a quarter of all cases that would formerly have required general anesthesia, and no fatality was reported with these methods. Kümmell reports only 0.61 per cent. of postoperative pneumonias in contrast to 2.5 per cent. formerly, and von Eiselsberg only 0.9 per cent. instead of 3.3 per cent. formerly. Neuber (Archiv f. klin. Chir., Bd. lxxxix, Nu. 4, 1909).

The above figures probably give an incorrect idea, however, of the relative danger of chloroform anesthesia in warm climates, such as exist in the southern United States, and probably under certain other circumstances. Thus Lawrie has reported 30,000 chloroform anesthesias without a death, and Dastre reported only 1 death in 11,448 chloroform administrations during the Crimean war (Gwathmey). Chloroform with oxygen in a southern climate is considered by Gwathmey a very safe anesthetic; he thinks also that in the northern United States chloroform is safer in the summer than in the winter. The same author gives the following table showing the mortality of various anesthetics according to statistics obtained from 99 hospitals in this country and including the years 1905 to 1911:—

Anesthetic.	Total of Anesthesias.	Number of Deaths.	Ratio of Deaths.
Local anesthesia	14,878	0	0–14,878
Nitrous oxide with oxygen	8,585	0	0– 8,585
Anesthol-ether	3,827	0	0– 3,827
Ethyl chloride	905	0	0– 905
Nitrous oxide with air	561	0	0– 561
Spinal analgesia	521	0	0– 521
Anesthol-ether-chloroform	153	0	0– 153
Anesthol-chloroform	123	0	0– 123
Nitrous oxide-ether-anesthol	114	0	0– 114
Essence of orange-ether sequence	100	0	0– 100
A. C. E. or C. E. mixture	95	0	0– 95
Ether-chloroform sequence	94	0	0– 94
Nitrous oxide-anesthol	45	0	0– 45
Ethyl chloride-anesthol	41	0	0– 41
Anesthol-oxygen	37	0	0– 37
Ethyl bromide	20	0	0– 20
Ethyl-chloride-oxygen	13	0	0– 13
M-H-C anesthesia	9	0	0– 9
Chloroform-ether sequence	16,054	2	1– 8,027
Nitrous oxide-ether sequence	41,435	6	1– 6,905
Anesthol	6,139	1	1– 6,139
Ether, drop or vapor	**157,453**	**28**	**1–5,623**
Ethyl chloride-ether sequence	4,431	1	1– 4,331
Chloroform-oxygen	4,009	1	1– 4,009
Chloroform, drop or vapor	**16,390**	**8**	**1–2,048**
Nitrous oxide	1,314	2	1– 657
Rectal anesthesia	516	1	1– 516
Intratracheal insufflation	1,000	4	1– 250
Nitrous oxide-ether-chloroform	183	1	1– 183
	278,945		

Of the eight chloroform fatalities shown in the table four occurred in the United States Army and the localities in which they took place are not known. Of the other four all occurred in a northern climate. Gwathmey concluded that chloroform is approximately 2½ times as dangerous as the nitrous oxide-ether sequence.

> For routine work, ether, by the open or drop method, is the safest and most satisfactory anesthetic. In the usual run of cases it is the anesthetic of choice in from 75 to 80 per cent. of the cases. Possibly in a laryngectomy the direct introduction of chloroform vapor into the trachea might produce less irritation to the tracheal mucosa with less risk of pneumonia than ether. Nitrous oxide is the anesthetic of choice for short operations, manipulations, and examination, as well as in operations on patients with seriously impaired kidneys and often in cases in extremely bad condition, as typhoid perforation, general peritonitis, etc. But it should not be employed in patients with bad hearts. It is not so satisfactory an anesthetic as ether, and should not be employed in preference to ether in patients who are good surgical risks. Bevan (Jour. Amer. Med. Assoc., Dec. 2, 1911).

CONTRAINDICATIONS. Respiratory Disorders.—Numerous cases of pneumonia following the administration of ether have been reported, and it is well known that ether causes decidedly more irritation of the respiratory passages, where inflammation of these is present, than chloroform. For this reason, ether is contraindicated in acute affections of the lower respiratory passages. In chronic disorders such as bronchitis, with profuse secretions, pulmonary emphysema and tuberculosis, chloroform is preferable to ether, except where the heart is weak. Asthma, goiter, and all other conditions tending to reduce the lumen of the bronchial tubes or trachea are to be looked upon as compromising factors in ether anesthesia.

> Diseases of the larynx and trachea require chloroform or chloroform mixed with ether. **Bronchorrhea,** pulmonary and pleural diseases, if active and progressive, indicate chloroform or **chloroform**-ether; if stationary, ether may be used cautiously. Recent pulmonary disease indicates chloroform or **C. E.**-ether sequence. The ether should be given most carefully and preferably drop by drop, so as to give exactly the required quantity and no more, with a bag cone, so as to warm the fumes as much as possible. When respiration and circulation are interfered with by such conditions as ascites and empyema, great care is necessary; ether should always be at hand if chloroform is being used, so

that if the evacuation of the fluid changes the condition of the circulation, it may be employed as a stimulant. In empyema, if the lung itself is no longer diseased, ether alone may be used. In both **ascites** and **empyema** much danger will be avoided if the fluid is aspirated a few hours before anesthetization. Pedersen (Med. Record, Feb. 11, 1905).

Ether is taken by young **children** very well for short operations if it is carefully given, but as the body temperature may be lowered from ½° to 3° F. very quickly, and that loss is very serious, one should hesitate before giving ether to a very young child. Some years ago the author tested the effects of giving ether to young children, and the main points which struck him were the liability to salivation and bronchorrhea, which he regarded as not only distressing, but injurious to the children. Of course for very brief operations one would employ nitrous oxide or ethyl chloride. During the operation of **circumcision,** except in extremely young children—babes a few weeks old—the writer always employs ether for the induction of anesthesia and continues with chloroform. Buxton (Proceed. Royal Soc. of Med., April, 1910).

Cardiovascular Disease.—In advanced arteriosclerosis and aneurism ether is relatively contraindicated because of the fact that the rise of blood-pressure it produces may result in rupture of a vessel.

From a study of 143 cases of anesthesia in the presence of heart disease, the author concludes that in the myocardial affections only do anesthetics exert any markedly bad effects. In valvular disease their influence is very slight, but yet appreciable. In functional disturbances it is insignificant. J. M. T. Finney (Amer. Jour. Med. Sci., Aug., 1901).

In subjects having high blood-pressure from atheroma or arterial sclerosis, chloroform in the hands of one skilled in its use should be the drug of choice, since the excitement is so much less marked. After the patient is once anesthetized the ether drop method may be tried, though often these subjects will not be controlled thereby on account of slow absorption, which keeps the patient just at the stage between excitement and complete anesthesia, manifested by irregular and explosive breathing and struggling. These subjects require large amounts of chloroform and comparatively large amounts of ether to control them, and furthermore, ether produces secretion of mucus in a much greater degree than chloroform. In a large majority of patients the **chloroform-ether** sequence will be found a safe and reliable anesthetic. If there be no contraindication, a mild dose of **morphine** and **atropine** should be exhibited—⅛ to ¼ grain (0.008 to 0.016 Gm.) of the former and ¹⁄₂₀₀ to ¹⁄₁₀₀ grain (0.0003 to 0.0006 Gm.) of the latter for an adult patient. Wenger (Detroit Med. Jour., Oct., 1909).

It is difficult to predict how a patient with heart disease will stand an operation. The nature of the lesion counts for far less than the degree of compensation. This applies equally to valvular lesions and to myocardial insufficiencies, though in the latter it is much harder to judge the exact condition. When it is known that a heart lesion exists, the anesthetist usually exercises extreme care, and this appears to be of great benefit to the patient. The use of large quantities of anesthetic within a short time seems to be particularly dangerous. Irregularities of the heart, with one exception, do not appear to be of great importance in giving anesthetics. Extrasystoles usually disappear during the operation and may not return for days afterward. The permanently irregular heart with delirium cordis, however, often causes alarm and the pulse becomes very fast. A patient with Graves's disease and this irregularity died shortly after operation. A. W. Hewlett (Phys. and Surg., Mar., 1910).

The author has had more trouble with operations and anesthetics **in** septic patients where the heart muscle has been weakened by absorption than in cases of valvular lesions. It is advisable to shorten as much as possible necessary operations upon such septic patients and the minimum amount of anesthetic should be given. Excessive adipose tissue is a distinct contraindication for some operations like the Wertheim operation for the radical removal of cervical cancer. R. Petersen (Phys. and Surg., Mar., 1910).

Any patient with a full, bounding pulse, high blood-pressure and plethoric appearance, with heavy specific gravity of the urine and excess of uric acid and urates, will, in the absence of heart lesion, take chloroform better than ether. Ingle (Amer. Jour. of Surg., July, 1911).

Renal Disease.—The presence of acute renal disorder or of chronic parenchymatous nephritis is a contraindication to ether, which is held to be more irritant to these organs than chloroform on account of the much larger quantity used (in spite of the fact that, volume for volume, chloroform is the more irritating of the two). Ether tends to diminish the quantity of urine, while chloroform tends to cause a marked post-anesthetic increase in the urinary flow. This difference doubtless depends on the difference between the two drugs in their action on the vessels of the splanchnic area, chloroform causing dilatation, while ether tends to constrict. The fact that many renal cases are arteriosclerotic is frequently an additional contraindicating factor with respect to ether. Albuminuria is caused by ether much oftener than by chloroform, though glycosuria is less frequently produced.

Opinions are by no means unanimous as to the superiority of chloroform over ether in renal cases. In cases with heart weakness, the latter might be preferable.

In nephritis, the choice of some other method than the inhalation of ether or chloroform should be considered, and, if at all possible, the method that has no injurious effect on the kidneys should have the preference—scopolamine-morphine narcosis, nitrous-oxide gas combined with oxygen, or lumbar analgesia. Boldt (Med. Record, May 29, 1909).

Diabetes Mellitus.—Both ether and chloroform are definitely contraindicated in the presence of the disease, as either is likely to bring on coma. Nitrous oxide anesthesia, with or without oxygen, or local anesthesia, is far preferable for these cases.

Anemia.—Pronounced anemia, *i.e.*, where the hemoglobin percentage is at 50 or below, contraindicates ether.

In operations upon the nose and mouth, ether, as commonly employed, is disadvantageous owing to the necessity of more constant administration of the anesthetic than in the case of chloroform, as well as on account of the greater irritation of the mucous membranes and more profuse flow of mucus and other secretions induced. By the use of intranasal tubes for the introduction of the anesthetic these drawbacks of ether can in part be avoided.

In many intracranial operations, ether is contraindicated because the rise of blood-pressure it causes induces congestion of the local vessels, which, in turn, leads to an annoying amount of hemorrhage.

Patients in whom, upon previous administration of ether, the latter has caused untoward pulmonary or renal symptoms, should not be given this drug at subsequent operations.

STAGES AND CHARACTERISTIC PHENOMENA OF ETHER NARCOSIS.—The effects of ether in the course of anesthesia may be divided, from the clinical standpoint, into several stages:

1. The stage of mental confusion or impaired consciousness, in which there is at the start a subjective feeling of general warmth, sometimes a choking sensation, and smarting of the nose and throat. Soon after the senses of sight and hearing become obtunded, tinnitus may be experienced, and a sensation of stiffness in the limbs may come on. The irritation of the mucous membranes by the anesthetic causes a greatly increased secretion of mucus and saliva. The patient becomes mentally confused, but when spoken to loudly may understand what is said and respond. The pulse is increased in strength and rapidity, and the respiration may be slightly accelerated. Even before consciousness definitely disappears, peripheral sensibility may be lost. There occurs a period of "primary anesthesia," during which small operations, such as opening an abscess, may be performed, or the pains of labor in parturient women obviated. The patient may become hilarious soon after the administration of the anesthetic is begun, but the exhilaration usually marks the advent of the second stage.

> Under certain circumstances it is very useful to employ partial anesthesia. Chloroform is better adapted than ether, as the latter is apt to cause a sensation of choking, and is not so quick in acting. After about two minutes, when the patient has inhaled from 80 to 100 drops, the sensibility for pain will be found to be almost absent, although he knows what is happening. The author usually makes the patient count during the inhalation, and as soon as there is the least irregularity in the counting it is time to begin. When there is an idiosyncrasy against chloroform, ether is used. The method is of great value in reducing **fractures,** especially of the radius and fibula, and in **dressing wounds** after operation, when plugging is required. Riedel (Berl. klin. Woch., July 7, 1902).
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> The author pours 3 to 5 Gm. (1 to 1½ drams) of ether into the cone and, after the patient has taken 10 to 15 deep inhalations, the operation can begin. He terms this method "one-minute anesthesia," since in many cases the operation can be started in about a minute after the first inhalation is taken. He has used the method in about 200 cases. To get the best results, not only as to safety, but efficiency, the patient must be kept in the narrow zone between the stages of sensibility and excitement. The patient counts after the anesthetizer, who occasionally changes the order of the numbers, and the minute the correct answers cease the anesthetic should be stopped and the operation begun. During the operation the anesthetizer should frequently urge the patient to count, and, if he responds, a little more anesthetic should be given, but not otherwise. If signs of excitement or resistance appear, stop the anesthetic and the operation for a minute or so, until the patient will count again. The advantages of the method are: (1) the decrease of danger; (2) the saving of time; (3) the saving of pain; (4) comparative absence of after-effects. Vomiting is very rare during or after the anesthesia; where nausea occurs, it is of short duration and very trifling. Clifford (Western Med. Rev., Nov., 1904).
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> Using a mask allowing free access of air, the author commences to operate as soon as the patient ceases to distinguish between a prick and a touch on the arm, or ceases to reply to questions. He uses from 5 to 15 Gm. (1½ to 5 drams) of ether, very seldom requiring 20 or 25 Gm. (7 or 8½ drams).

The patients often cry out as the operation is commenced, but this is not accompanied by any defensive movements; it is more the result of suggestion than of any actual sensation of pain, owing to the loss of self-control from the ether. The patient still has consciousness enough at the beginning of the operation to open his mouth or the like when told to do so; he is aware of the operation as it proceeds, but experiences no pain, merely the sensation of contact, and as soon as the operation is concluded can arise and, though in a somewhat exalted mood, feels perfectly well. Sudeck (Münch. med. Woch., Bd. liii, Nu. 41, 1906).

The special sense organs become inactive in ether anesthesia long before general consciousness is lost. Vision and audition cease before touch and sense of position. A feeling (anguish or anger, etc.) is the most persistent mental state. In the process of gradual recovery of normal consciousness feeling is first reinstated. Purely intellectual activity, without images, is next in order. Vague tactual sensations, pressure, and sense of position return before sight and hearing. Johnston (Jour. of Abnormal Psych., April-May, 1909).

Many small operations can be performed in the first stage of ether narcosis: it is only necessary to instruct the patient to breathe deeply seven to eight times, and then press a mask saturated with 10 c.c. (2½ drams) of ether firmly upon the face. The anesthesia lasts from five to ten minutes, and is not usually followed by nausea or other after-effects. W. Busse (Therap. d. Gegenwart., May, 1909).

The writer has found it possible to prolong to an hour or more the stage of incomplete anesthesia in which sensibility is abolished, but the patient is still able to respond to questions, give his name, and look around—*Ætherrausch.* He has performed major operations on the legs, abdomen, etc., with this anesthesia, the patients lying quiet, babbling unintelligibly and moving their heads, but otherwise not interfering with the progress of the operation. L. Moszkowicz (Zentralbl. f. Chir., Feb. 5, 1910).

The author has performed 35 **laparotomies** under primary ether anesthesia alone, never letting the patient pass from the stage of "drunkenness" to that of agitation, and only giving a few drops when there are signs of returning consciousness. He has also applied the technique in 5 **hysterectomies, 45 herniotomies,** in transvesical **prostatectomy,** numerous **gynecological operations** and **operations on bones** and **joints.** No fatality has been known with this method since Sudeck introduced it. The analgesia can be prolonged for an hour and a half or longer. There is less danger of postoperative pneumonia, as the patient can swallow as saliva collects in his mouth, while the less quantity of the anesthetic used reduces danger from this source. The only disadvantage is that the patients may move and disturb the operator, but a few drops of chloroform overcome this. Mariani (Gaz. degli ospedali, Nov. 15, 1910).

The author describes the ether *Rausch,* or primary anesthesia, which may be given in a variety of ways. The air must be excluded as much as possible. The author has used a couple of wet towels rolled in the form of a hollow cylinder or cone, with an ether-saturated towel or cotton-wool over the upper end. Often he has used an ordinary derby hat. This is made to fit the patient's face closely by means of wet towels placed around the edge, and wet towels are placed around the sides and over a portion of the top; the wet towels exclude the air better. He has tried the ordinary open mask in many cases, but never found it satisfactory. Having used the *Rausch* more than 200 times, he recommends its use in all minor surgical operations. He has used it in opening **abscesses,** setting **fractures,** reducing **dislocations,** removing **ingrown toe-nails,** etc., but does not use it where the operation requires more than five minutes' time to perform, or in those in which general relaxation is necessary. Coughlin (Jour. Amer. Med. Assoc., July 1, 1911).

2. The stage of excitement, in which, owing to the probable primary stimulating effect on certain portions of the brain, the patient acts, especially if the ether be given too rapidly, as if he were intoxicated with alcohol, struggling more or less violently and sometimes shouting, laughing, singing, etc. He often tries to remove the gauze or inhaler and to rise from the table. Hallucinations are frequent during this stage, and when ether is administered to a woman, a third party should invariably be present. The heart action in this stage is decidedly accelerated, while the respiration may be irregular, presenting an alternation of complete suspension for a longer or shorter time, owing to reflex inhibition from the irritated respiratory passages, and of compensatory deep and rapid respirations, which tend to bring about sudden introduction of a large amount of the anesthetic. The skin is flushed, warm and moist. The pupils are generally dilated, but the pupillary light reflex, as well as other reflexes, are still present.

3. The stage of completed surgical anesthesia, in which, in addition to entire loss of consciousness, the function of all reflex mechanisms, including those of the spinal cord, is at a standstill. (Since Crile has shown that continued violent stimulation of sensory nerves may produce abnormal changes in the cells of certain centers, the statement that ether anesthesia totally abolishes central activity is no longer warranted). In this stage, the muscles are relaxed, the arm dropping when raised. The pulse under ether is still accelerated and of full volume. The respiration is regular, slow, fairly full, and sometimes noisy, in which event the head should be turned laterally in order to cause the uvula to drop to one side and the diameter of the passage to increase. As the period of anesthesia increases the breathing becomes gradually shallower, and rarely, in long procedures, markedly feeble and once more irregular. The skin in this stage is moist and suffused as before. The pupils are contracted as in normal sleep, and the reflexes, at the beginning of the third stage, disappear in the following order: (1) Patellar. (2) Reflexes of coughing and swallowing. (3) Corneal and conjunctival reflexes. The pupillary light reflex is retained, though the pupil is small. The temperature is slightly lowered — less than with chloroform.

When the ether is stopped at the end of the operation, the patient, in recovering, may pass again through the stage of excitement, though this is regularly milder and shorter than in the beginning. The patient often vomits, probably partly because of the irritation of the pharynx and stomach by the ether, and then falls asleep.

4. The stage of danger or collapse, where too much ether is administered or the anesthesia excessively prolonged. Here the pulse becomes weaker and more rapid than before, and may not be felt at the wrist The respiration is shallow, slow and often stertorous, owing to complete relaxation of the muscles of the soft palate. The skin is cold and livid. The

pupils are dilated, with the light reflex abolished. The temperature is clearly subnormal. Loss of muscle tone is even more complete than in the stage of surgical anesthesia, and the limbs are in an entirely limp condition. Death, if it occurs, usually results from failure of the respiratory center.

METHOD OF ADMINISTRATION.—Preparation of the Patient.—Examination of the patient's urine, circulatory system, and if anemia be suspected, of the blood, are prerequisities to a well-conducted anesthesia. The urine should be examined as to amount and for the presence or absence of albumin and casts. Where the amount is subnormal, free administration of water, with or without saline diuretics, is advisable (Hare), while if casts are found in large number, or sugar is present, ether anesthesia is contraindicated.

Where cardiac disease, especially of the valvular variety, is not so marked as already to give rise to pronounced symptoms of insufficient heart function, the administration of some such drug as **strophanthus** has been advised.

In the presence of a hemoglobin percentage lower than 50, ether should be given only in case of great necessity, in view of the destructive action of the drug on the red cells. Some surgeons, however, have placed the danger limit at 40 per cent. The administration of oxygen is of value during and after anesthesia of seriously anemic patients.

Plenty of nutritious and easily digested food should, if possible, be supplied to the patient until the day before the operation, when the diet should be made light. No solid food or milk should be allowed within several hours of the anesthesia, but water and gruels may be given to within two or three hours of it.

> **Glucose** is valuable both before and after operations, not only to prevent or combat acid intoxication, but as a food which makes no call on digestion. A tablespoonful can be given with water and lemon-juice three times or more in the twenty-four hours, or in special cases it may be given by the rectum or intravenously (2.45 per cent). Mortimer (Lancet, June 17, 1911).

Mellish advises that **castor oil** be given at least twenty-four hours before the operation, so that the patient will not be depleted of fluids before the intervention. An enema is then given a few hours before the anesthesia. Other surgeons administer only a mild **aperient** some hours before the operation.

The mouth should always be examined previous to inhalation anesthesia, and such foreign bodies as detachable false teeth, food remnants, chewing gum and tobacco should be removed.

> Any plate containing artificial teeth should be removed from the patient's mouth if it is so small that if dislodged it might prove dangerous either by being swallowed or lodging in the gullet. But a complete set or sets should not be taken out, as swallowing or choking is out of the question, and upon removal, the cheeks and lips so fall in as to encroach, in some patients, to a serious degree on the breathing space within the mouth. Dawbarn (Jour. Amer. Med. Assoc., April 21, 1906).

It should also be made a rule to wash out the oral cavity with an efficient antiseptic solution, *e.g.*, a dilute **potassium permanganate** or **hydrogen dioxide** solution.

The author insists upon the importance of preliminary thorough disinfection of the mouth by inhalations of **thymol** and by **salicylic acid** with alcohol and hot water; this is done on the preceding night and just before operation. The antiseptic inhalations are resumed as soon as the operation is completed. This method materially lessens the after-dangers of etherization. Pneumonia induced by etherization is of a different type to the usual form, with lower and less regular temperatures and without the appearance of a true "crisis." The pulmonary signs develop later and there are less cough and sputum. In prophylaxis, stress is laid upon strict limitation of the quantity of anesthetic inhaled and attention to the posture of the patient. A. Otte (Lancet, Dec. 26, 1908).

Any tight clothing over the neck and chest should be loosened before beginning the anesthesia.

The induction had best be conducted in a quiet room. No talking, except to the patient, should be allowed during this period, and no attempt to move the patient should be made in the early stages of the anesthesia. Care should be taken by the anesthetizer to gain his confidence and allay any fears of the anesthesia he may have entertained.

It often happens that only toward the close of an operation is the patient's abdomen in a perfectly satisfactory condition of relaxation from the surgeon's point of view. It is well, therefore, in abdominal cases, to let the anesthetist get to work at the earliest possible moment—as soon, for instance, as the surgeon begins to get his instruments ready. Blumfeld (Lancet, May 31, 1902).

During the first stages of the induction of anesthesia fear may be an important factor in causing a catastrophe. A nervous boy, aged about 9 years, was to have his tonsils and adenoids removed under chloroform. He was placed on tne table, and a relative was holding his hand. The mask was held before his face, and before any chloroform was poured on it the patient began to breathe rapidly, drumming with his heels on the table, and saying "I'm going." The anesthetist tried to quiet him and told him that he had as yet had no anesthetic, but the rapid breathing continued for a few seconds, and the boy died. Nothing abnormal had been found in the chest before the administration. No *post mortem* was allowed. R. J. Probyn-Williams (Clinical Journal, Dec. 23, 1908).

Moistened gauze or cotton may be placed over the patient's eyes during the administration.

Protection of the eyes in anesthesia is most satisfactorily accomplished by taking small pledgets of absorbent cotton, placing them over the eyes to absorb the tears, and over this a piece of rubber dam large enough to cover both eyes and extend over the eyebrows, with a vent to allow of protrusion of the nose, and which closely adheres to the skin of the face. Over all is placed a flat piece of absorbent cotton of the same shape and size as the rubber dam, with a slit for the nose. This absorbent will catch any drops that may accidentally fall on the face. Samuel Johnston (Can. Pract. and News, Mar., 1912).

Exclusion of two or more extremities from the general circulation during anesthesia has been advised by Klapp and others.

With the application of constricting bands high on the thighs, thus damming off part of the circulating blood, far less of the anesthetic is required. The author first applies a constricting band to collect a certain amount of blood in the legs and then over this applies a tourniquet to shut off the blood as effectually as with an Esmarch bandage. He orders the patient to breathe deeply and tranquilly; the room should be perfectly still. Then from 10 to 20 c.c. (2½ to 5 drams) of ether are given all at once, which is enough for fifteen minutes' anesthesia. For longer operations he gives from 20 to 30 c.c. (5 to 7½ drams) at once, and then 10 c.c. (2½ drams), continuing with the drop method. Klapp (Therap. Monats., Jan., 1910).

Klapp's method applied. Six patients developed thrombosis among the 75 laparotomized. None of the patients was subject to varicose veins. The thrombosis in the leg in each case was transient and harmless, but it has convinced the author that this method has too many dangers. The thrombosis developed exclusively after laparotomies, nothing of the kind having been observed after 110 vaginal operations. Gräfenberg (Deut. med. Woch., Feb. 3, 1910).

Klapp's method used in 71 cases. Thrombophlebitis developed in 3 cases. With part of the circulation shut off the tendency to vomiting ceased to be materially reduced, but this advantage was counterbalanced by the sense of weight and tingling in the legs in the first few days after the operation. In the 3 cases in which thrombophlebitis developed the constriction had been applied for from sixty to seventy-two minutes; the operations were for hernia or ankylosis of the knee. Donati (Riforma medica, March 14, 1910).

Report of 63 cases in which an Esmarch bandage was applied to the legs or arms or both to exclude these members from the general circulation. The amount of chloroform necessary for major operations thereafter was much lessened. The first phase of anesthesia was shortened, the nerve-centers feeling the effect of the anesthetic remarkably early, and the patients rousing afterward much quicker. No by-effects were observed. Berri (Gaz. degli ospedali, May 22, 1910).

Upon contracting the circulation during general anesthesia by applying tourniquets to the extremities, there is less bleeding in operations on the head, neck, and trunk, and even on a nonobstructed part of an extremity. The method may be applied for hemorrhages occurring during childbirth and internal hemorrhages. The author applies the small rubber tube near the axilla and groin under slight tension before beginning the anesthetic. He withholds the chloroform until there is a bluish-red congestion of the extremities. The veins are almost completely obstructed by the tourniquet and the arteries only partially, the back pressure completing the blockage in them. Hans (Zentralbl. f. Chir., Bd. xxxvii, S. 1579, 1910).

Klapp's technique employed in 1144 cases, using chloroform, and in 35 with ether. When the constriction was removed, the blood and tissues excluded from contact with the anesthetic diluted and took it up rapidly. The patient roused at once or in about ten minutes, and the postanesthetic disturbances were reduced in frequency and intensity. In case of accident, removing one or more of the bands flushes the system with fresh blood and starts up the respiration anew. The members feel a little numb or there may be minute ecchymoses. Postoperative phlebitis developed in 4 cases. Heart and vascular disease or general infections may contraindicate the method in certain cases, but it has special advantages in all cases of kidney and liver disease. Delagénière (Bull. de l'Acad. de Méd., July 25, 1911).

Posture.—The patient's head may either rest on the table or be somewhat elevated by a firm pillow, in order, as much as possible, to remove tension from the anterior tissues of the neck and facilitate breathing. Where there is pus on one side of the thorax the patient should always be turned upon that side during anesthesia, in order that the opposite lung may be wholly unhampered in its work, as well as to prevent any pus from entering the bronchus of the sound side (Probyn-Williams).

Stress laid on comparative frequency of paralyses of the brachial plexus after operations in Trendelenburg's posture which, the author believes, are due to pressure exerted on the plexus at a point between the clavicle and the first rib. In addition he has noted minor disturbances such as temporary numbness, crawling sensations, etc. All these unpleasant phenomena can be avoided by arranging the arms in a proper manner and at the same time noting the amount of compression to which the arteries are subjected. The pulse at the wrist is a valuable guide. The arms should be fastened to the sides, below the table, with a cushion under each arm. Rothe (Zentralbl. f. Gynäk., Nu. 12, 1904).

The author recommends, in vaginal operations, placing the arms across the chest and keeping them in position by winding the lower part of the sheet under them. In laparotomies, the arms are crossed under the back. In this manner, they are kept from hanging over the edge of the table with the possible result of a pressure paralysis. Preschnig (Zentralbl. f. Gynäk., June 25, 1904).

Patients with any pre-existing respiratory affection should not, as a rule, be placed in the Trendelenburg posture. F. W. Hewitt (Lancet, Aug. 10, 1907).

While a patient is in the Trendelenburg position the percentage of decrease in the excretion of urine is 58 per cent. in ether anesthesia and 82 per cent. in anesthesia by chloroform. This great decrease is not, even in moderate degree, due to urine being retained in the renal pelvis; nor to unsatisfactory drainage by the catheter. In renal inefficiency and cardiac and arterial lesions it seems that the use of the Trendelenburg position introduces a special element of danger, and this less markedly when ether is used than when chloroform is employed. Bovée (Amer. Jour. Med. Sci., Jan., 1911).

In operating upon the nose and throat the two main reasons for desiring the upright position are: First, that more skillful and therefore more satisfactory work can be done when one can make use of the same topographical relationship with the patient as that to which one is accustomed in every-day, office practice. Second, that in any operative work about the head less blood is lost when the patient is upright. In routine operations performed in the nose and throat, even without alertness in sponging, embarrassment from blood flowing into the windpipe does not occur.

The elevation of the body from the recumbent to the upright position should be made slowly. The secret of a safe and uninterrupted administration of an anesthetic in the upright position is in keeping the neck somewhat stretched and the head moderately extended over the head-rest. T. R. French (N. Y. Med. Jour., Mar. 16, 1912).

Preliminary Medication.—**Morphine sulphate,** 1/8 to 1/4 grain (0.008 to 0.016 Gm.), and **scopolamine hydrobromide,** 1/200 to 1/100 grain (0.00032 to 0.00065 Gm.), are not infrequently given hypodermically in a single or in divided doses in the two hours preceding anesthesia. The combination acts as a decided adjuvant to the action of the ether, reduces the amount of the latter to be administered, places the patient in a drowsy state previous to operation, and tends to prevent excitement during the induction. Its disadvantages are, that it renders observation of the pupil practically valuless in judging of the depth of anesthesia, and that the patient remaining narcotized some five or six hours after the end of the operation, constant watching is necessary during this entire period. The method should not be used in cases of heart disease, and must be employed only with caution in aged persons as well as in the young.

The author favors the routine administration of **morphine** in small amounts, except in respiratory difficulty, coma, great weakness, anemia, and extreme old age. It is useful both with chloroform and ether, but is safer with ether because of the stimulating effect of ether on the respiration. The possibility of an idiosyncrasy to opium and its derivatives must, of course, be kept in mind. All athletes and alcoholics should have this preliminary dose of morphine. Whenever it is used, a lighter grade of narcosis should be maintained than when it is not used. All or the majority of the fatalities that have occurred, especially with scopolamine and morphine, have been due to neglect of this rule. If **ethyl chloride** is used to induce anesthesia it is safe to follow it with ether, but very unsafe to follow it with chloroform. It is legitimate to start with ethyl chloride, then to switch to ether, and if the reflexes are only slightly in abeyance, to follow with chloroform. In giving ether or chloroform alone, most of the reflexes must be abolished to keep up the proper degree of anesthesia, but if morphine is administered these reflexes may be allowed to remain and yet the patient will be perfectly quiet. J. T. Gwathmey (Jour. Amer. Med. Assoc., Mar. 28, 1908).

It is of great importance to insure complete cardiac rest the night before an anesthetic is given; hence the author always administers 15 grains (1 Gm.) of **veronal.** One hour before the operation 15 to 20 mgm. (¼ to ⅓ grain) of **morphine** are injected, and the patient receives an enema of 75 Gm. (2½ ounces) each of cognac, red wine, and tea.

For narcosis, the author uses ether by the drop method, on an Esmarch mask. With alcoholics it may be necessary to employ **chloroform** at first, but ether should be substituted later. Strauch (Med. Klinik, Nu. 10, 1908).

Scopolamine and **morphine** used in 132 cases before ether. One-half grain (0.03 Gm.) of scopolamine is accurately weighed and dissolved in 25 drams (100 c.c.) of sterile water. One dram (4 c.c.) of this solution is put into a sterile vial, and ½ grain (0.03 Gm.) of morphine sulphate is added. Each bottle contains 1/50 grain (0.0012 Gm.) of scopolamine and ½ grain (0.03 Gm.) of morphine, the amount of three injections for one patient. These vials are not used after five days. One-third (20 minims—1.25 c.c.) is given hypodermically two and one-half hours before operation, a second similar dose one hour later, and the remaining one-third one-half hour after this, or one-half hour before operation. One responsible nurse has charge of the administration. After the first injection the pulse and respiration are carefully watched. If there is a marked disturbance of the pulse rate or rate of respiration, or the pulse becomes irregular, the second and third doses are omitted. The same holds good after the second dose. The object is not to produce profound narcosis, but drowsiness or light sleep. Some patients are easily influenced by one dose; others come to the operating room after the third dose wide awake. Practically all are able to help themselves on to the operating table from the stretcher. The face is usually flushed, the lips dry; the pupil sluggish, usually slightly contracted, occasionally dilated. The patient is easily aroused; the speech is slow and occasionally incoherent. In only 2 cases has the author observed any initial excitation. The preparation of the patient is started before the ether is administered and the anesthetist always waits until the surgeon and his assistants are ready, or nearly so, so that no time may be lost after the anesthesia is complete.

The following conclusions were reached: In 102 cases the average period of induction was eleven minutes. The excitement stage is practically eliminated. Vomiting during operation is rarely seen. There is no secretion of mucus and the respirations are as noiseless as in chloroform anesthesia. The respiration is considerably checked and, consequently, dehydration of the body is diminished. The amount of anesthetic is markedly reduced. In 131 cases the average amount of ether per hour was exactly 4 ounces (120 c.c.). The patient usually sleeps a considerable time after the operation and is thus relieved of the initial pain and vomiting. Forty-two per cent. had no postoperative vomiting. The anesthetic may be withdrawn for considerable periods during the operation and almost always after the closure of the peritoneum. In 1 case (a vaginal hysterectomy) it was withdrawn for fifty-five minutes. In another (the removal of a large cyst) the patient went fifty minutes without ether. In none of the cases was there pneumonia or bronchitis. The scopolamine-morphine mixture is of much advantage in nervous women undergoing abdominal or pelvic operations and in whom there is no contraindication. R. Maurits (Physician and Surgeon, Mar., 1910).

Protest against the routine giving of drugs before ether and chloroform anesthesia. In cases of any untoward accident, there is not only the volatile and quickly removable drug, but also the non-volatile and comparatively permanent one to be eliminated. **Morphine** allays the reflex excitability of the air-passages, thus retarding coughing and favoring the retention of aspirated blood or vomitus in the trachea or bronchi, which predisposes to pneumonia. Many people are unable to take morphine without distress or vomiting, and in such individuals the disagreeable after-effects of ether or chloroform would be aggravated. If the lovers of **atropine** will keep the patient's head turned to the side, troublesome mucus will escape at the angle of the mouth or remain in the cheek, where it can be wiped out. Isabella Herb (Jour. Amer. Med. Assoc., May 6, 1911).

Recommendation that a deep subcutaneous injection of **omnopon** be given an hour previous to operation. When the patient is placed on the operating table, he is slightly sleepy. Upon putting the mask over the nose and mouth, in about three minutes, as a general rule, and having administered from ½ to 1 ounce of ether, the patient is snoring comfortably and absolutely lax. No difficulty is experienced in maintaining this condition with another ½ ounce of ether for an hour. The pupils are slightly contracted and react to light. The author has noticed in some cases slight and temporary divergent strabismus. The conjunctival reflex is absent. The face is slightly flushed a pink color. The pulse is full and steady. The respirations are slow and deep, perhaps 12 to 15 a minute. There is no mucus production in the throat, and no spasm or tremor. Robertson (Lancet, Oct. 7, 1911).

The authors have used **hyoscine** and **morphine** in over 200 cases as a preliminary to general anesthesia in adults. The ordinary dose was hyoscine 1/100 grain (0.0006 Gm.), morphine 1/6 grain (0.01 Gm), atropine 1/180 grain (0.00035 Gm.), hypodermically, one to three hours before operation. In young women the dose of hyoscine was sometimes 1/200 grain (0.0003 Gm.). The majority of patients had the previous night 10 grains (0.6 Gm.) each of **trional** and **sulphonal.** Fifteen minutes after the hypodermic injection the patient is completely indifferent to his surroundings. He walks into the operation room (when his condition permits) without apprehension, is somewhat dazed, but replies intelligently to questions, usually takes the anesthetic without terror or struggling, and when he wakes up some hours later remembers nothing that has happened. Less of the anesthetic is required, the quieting effect on alcoholics is noteworthy, and postoperative vomiting is much less frequent. In no case were there ill effects. In cardiac cases the procedure adds an element of safety. The authors have not carried it out where there has been albuminuria. Darling and Williamson (Dublin Jour. of Med. Sci., July, 1911).

In cases of **goiter** and glandular growths pressing upon or displacing the trachea, the safest method, if ether is used, is to inject **atropine** gr. 1/100 (0.0006 Gm.), or this together with **morphine** and **scopolamine,** half an hour before giving ether by the open method. In this way a certain diminution of the bronchial secretion can in some cases be obtained. In large numbers of cases of goiter, both simple, malignant, and exophthalmic, the author has used chloroform in low percentage vapor with a copious stream of **oxygen.** This plan has answered extremely well, and possesses the great advantage that one can readily lighten and deepen narcosis as the steps of the operation demand. Buxton (Brit. Med. Jour., Nov. 4, 1911).

Indispensable in every surgical procedure of magnitude, in gas and oxygen anesthesia, and also in spinal anesthesia, is the preliminary use of **morphine, atropine,** and sometimes **hyoscine.** For the control of difficult subjects, *i.e.,* plethoric, alcoholic, athletic, or obese people, the author gives large preliminary doses of morphine and atropine, induces anesthesia with A. C. E. mixture or anesthol, putting the patient under rather rapidly in order to avoid a stage of excitement, and maintains anesthesia with ether on a semiopen inhaler, possibly giving **chloroform** or C. E. again toward the end of the operation. A very useful maneuver in these cases is to use nasal tubes. In heart cases the author generally uses the A. C. E. ether sequence with **oxygen.** Nitrous oxide and oxygen is the safest anesthetic if restricted to momentary administration. F. Allen (Boston Med. and Surg. Jour., Dec. 28, 1911).

All patients, except possibly those under 8 or over 80, should have preliminary medication. It is much easier to anesthetize a patient half-asleep than one with the reflexes all in rebellion. The tissues of the human body, after an operation lasting an hour or more, are in a condition that, if evil effects are to follow the use of ether or chloroform, they are apt to occur. Here **nitrous oxide** and **oxygen** should be introduced cautiously and quietly. The patient should be under the gas less than two minutes. The author does not believe in the drop method as a constant one. He uses it daily at some time in the anesthesia, but considers the vapor method with warm, attenuated, moist air its superior by far, and superior to the nitrous-oxide and oxygen method. At the close of every operation the patient should have from 1 to 2 pints (500 to 1000 c.c.) of warm **saline** with 1 ounce of **glucose** per rectum to relieve thirst and fill out the veins. As the operation is closing or a little later, an **enema** of 3 to 6 ounces (90 to 180 c.c.) of warm **olive oil** should be given to restore the opsonic index. With these precautions, not 1 patient in 10 will have any nausea, vomiting, or unpleasant recollections of the operation. J. C. Gwathmey (Jour. Amer. Med. Assoc., Feb. 17, 1912).

The author advocates a preliminary hypodermic injection of 1/100 to 1/120 grain (0.0006 to 0.0005 Gm.) of **atropine** three-quarters of an hour before ether is administered, since by this means excessive secretion of mucus in the respiratory passages is prevented, and there is less danger of cardioinhibitory shock. Where the patient is very nervous or there seems some special indication for it, morphine can be combined with the atropine. In most of their cases the authors obtain the best results by starting anesthesia with **chloroform,** administered drop by drop upon a Skinner mask. By this means nervousness and hyperthesia are dissipated. At the end of about two minutes the chloroform is replaced by a mixture of chloroform and ether (2 parts of chloroform to 3 of ether), which serves to still further deepen anesthesia. This mixture is also used for two minutes, and at the end of about four minutes the ether is used alone. Thus all struggling and excitement is avoided. The percentage of ether supplied to the patient when it is dropped upon a Skinner mask lies between 5 and 15, according to the freedom with which the drug is employed. If gauze is used in the inhaler it yields a higher percentage than lint or flannel, and the percentage varies roughly according to the number of layers. If the flannel or lint is so adjusted that all inspirations and expirations pass through it, a more or less even percentage, usually 8 to 9 per cent., may be depended upon. Hewitt and Symes (Lancet, Jan. 27, 1912).

If the dosage of **morphine** be confined to the lowest useful limit, say ⅙ to ⅛ grain (0.01 to 0.008 Gm.) for adults, with the usual dose of **atropine**, say 1/100 to 1/150 grain (0.0006 to 0.0004 Gm.), or **scopolamine** 1/100 to 1/150 grain (0.0006 to 0.0004 Gm.), and the anesthesia by open ether be not carried to too deep a level, marked respiratory depression will rarely occur. **Omnopon** (the total alkaloids of opium) appears to offer a way of obtaining the advantages of morphine in mixed narcosis with a diminished risk of respiratory depression. Clinical experience of omnopon, scopolamine, **nitrous oxide** and **oxygen** with ether, favorably impresses one. The after-effects are much less and the patient proportionately less unhappy on recovery. Much less ether is used than by other methods. Embley (Austral. Med. Gaz., Aug. 17, 1912).

By combining local anesthesia with a minimal inhalation anesthesia or with spinal anesthesia superior ultimate results are obtained. The vitality is not lowered so much and the patient leaves the table in much better condition than when the entire dependence has been on inhalation of the anesthetic. The author gives 0.01 Gm. (⅙ grain) of **morphine** half an hour before the operation, then anesthetizes the abdominal wall by the infiltration method. While waiting for this to take effect, the operator completes his own preparation and the field is sterilized. The patient is then ready for the ether and very little is required. Whatever method of anesthesia is employed, preliminary anesthetization of the abdominal walls proves a great help in reducing the amount of ether required. He has been experimenting with drugs to promote the relaxation of the abdominal walls to permit coaptation, but he knows of none that will produce this effect on local application. Löwen (Beiträge z. klin. Chir., Sept., 1912).

The use of various essential oils has been recommended to facilitate the induction of ether anesthesia. As far back as 1902, Briggs advised that 1 dram (4 c.c.) of the **oil of peppermint** or of a 50 per cent. solution of **menthol** in alcohol be sprinkled over the inhaler and respired by the patient for about three minutes before the administration of ether was begun. More recently Gwathmey has recommended the preliminary administration of **oil of orange**. The value of these oils, which recent experience seems to have confirmed, consists in rendering the induction more easy and rapid and the anesthesia "smoother" throughout, in overcoming all tendency to coughing and choking sensations, in suppressing or greatly shortening the period of excitement, and in diminishing the post-anesthetic vomiting. Mellish was able to corroborate the statements of Briggs concerning the efficiency of peppermint oil in these directions.

Before anesthesia, in cases in which embolism from thrombosis is not feared, injections of isotonic or paratonic **solutions of calcium chloride** or of sera containing **lime**, with or without admixture of **blood-serum**, are good methods to promote coagulation, increase blood-pressure, and reinforce heart action. After anesthesia, subcutaneous, intramuscular, or intravenous injections of a **glucose** or **levulose** solution dilute the anesthetic remaining in the organism, shorten its contact with the tissues, and thus diminish the toxic sequelæ. Fleig (Presse méd., Jan. 1, 1910).

Administration and Dose.—The apparatus used in administering ether ranges from the exceedingly simple to the decidedly complex. The *"open method,"* reduced to its simplest expression, consists merely in the placing of a number of thicknesses (8 to 12) of gauze over the patient's mouth and nose, and dropping ether in gradually increasing, then constant amount upon the gauze. A method formerly much, but now less, employed, consists in the use of a cone or cornucopia made with a towel supported by felt or pasteboard, the base of which rests over the face, and at the apex of which an opening is provided, which is filled with gauze, upon which the ether is dropped.

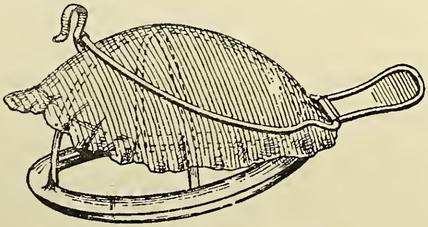

Fig. 1.—Schimmelbusch's mask.

There is a tendency to the excessive administration of ether and insufficient entrance of air with this method, which has led to the general adoption of different procedures.

Autoetherization used for twenty-five years. It increases safety and adds to the comfort of the patient. The patient assumes a sitting posture and etherizes himself in this position, which prevents embarrassment to breathing. The cone employed is made of leather and packed with cotton-wool. From 1½ to 2 ounces (45 to 60 c.c.) of ether is poured into the cone, which is handed to the patient with instructions to apply it closely to the nose and mouth and to take long, full breaths; if the vapor be too strong or a sensation of choking be experienced the patient is allowed to withdraw the cone. When the patient's hands drop, a brief operation may be performed or the anesthetizer may take the cone and continue the etherization. F. Buller (Montreal Med. Jour., Nov., 1902).

Many thicknesses of even wide-mesh gauze may soon become saturated with moisture, and thus offer as much obstruction to the passage of air as an almost impervious cloth. Should the fear be entertained that the thin gauze will not break the drop, a small tuft of cotton may be placed on the thinner gauze to receive and dissipate the ether. J. B. Bogan (N. Y. Med. Jour., Sept. 24, 1910).

Recommendation of the use of a cone about the size of a quart tomato-can, with ends removed and sides flattened enough to give an oval shape. The top of the cone is closed by laying several layers of gauze over it, and on to this gauze the ether is dropped. By the time the ether vapor traverses 5 or 6 inches of warm air space, and reaches the mouth and nostrils of the patient, it has been pretty thoroughly mixed with air and is warm.

The gauze roof of the chamber offers sufficient obstruction to the expired air so that at the beginning of inspiration the air chamber is full of expired air. The rebreathing aids in conserving the normal amount of carbon dioxide in the lungs and, therefore, in diminishing the danger of acapnia and shock. If the anesthetist wishes to concentrate the ether vapor, additional layers of gauze, permitting the use of more ether, may be employed or the cone may quite easily be closed, partially or completely, by a towel applied over the gauze top. C. P. Bull, Jr. (Med. Record, May 24, 1913).

The plan now most commonly followed involves the use of a wire frame or mask, such as that devised by Schimmelbusch (see Fig. 1), which is laid over the patient's face and covered with several layers of gauze. A piece of gauze tissue or other absorbent material, with an opening in the center which is placed over the mouth and nose, may with advantage be used beneath the mask, *i.e.*, in contact with the skin. The evaporating surface has to be larger for ether than for chloroform, and at least twice the number of layers of gauze is required for the former anesthetic.

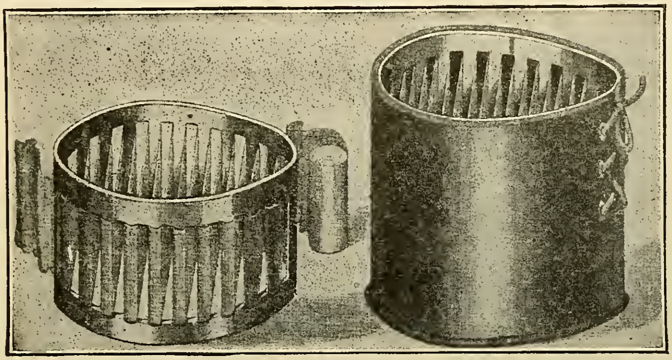

Fig. 2.—Allis's ether inhaler (*Fowler*). Showing fenestrated metallic frame with a muslin roller in course of application, and the inhaler complete with cover.

> Description of a cover devised for a drop-ether mask. It is made by quilting cotton between two layers of No. 2 gauze, cutting a hole one and one-half inches in diameter in the summit, taking out one or two wedge-shaped pieces at the base so as to cause the cover to fit the mask, and hemming all raw surfaces with tape.
>
> Ether is given by the drop method through a mask covered with gauze, slowly at first, and as soon as the patient becomes accustomed to the vapor the quilted cover is fitted over the mask, with the base carefully approximated to the patient's face, and the drug is then dropped on to the gauze through the aperture. By this method patients are put under and kept under the anesthetic with a minimum amount of drug, the anesthesia is much more uniform, and there is no need of winding roller gauze or a cumbersome towel about the mask. After each administration the cover should be washed and dried. C. G. Pearson (Jour. Amer. Med. Assoc., Nov. 23, 1912).

A still more perfect and widely used instrument is the Allis inhaler (see Fig. 2), provided with perpendicular, parallel linen partitions which allow a free passage of air to the patient, while also providing ample surface upon which to drop and vaporize the ether.

> The author uses the Allis inhaler. Just before beginning he places 3 pieces of sterile gauze on it, and in 2000 cases has had no pneumonia. The cone should be placed on the face with the head a little elevated so as to sit at an angle. The eyes are covered with a folded towel.
>
> He starts with 1 drop of ether, then in a second adds 1 more drop, then 2 drops, 4, 10, up to 30, and continues the 30-drop doses until anesthesia is complete, when a few drops every few seconds will keep a patient under. In alcoholics, or tobacco, cocaine, and morphine patients, the drop system will not suffice. To the opium and cocaine fiends he gives a dose of these drugs before beginning anesthesia. In swabbing out the throat moist-gauze sponge

should be used instead of dry. In cases of profuse perspiration during anesthesia the author gives 1/60 grain (0.001 Gm.) of atropine. G. Spencer (Amer. Medicine, July 11, 1903).

There are but few occasions in which ether may not be given *to children* in preference to other anesthetics. The most important of these is an abnormal state of the respiratory organs, as in acute bronchitis, pulmonary congestion or pneumonia. The open method should be adopted always. The smaller size of Allis's inhaler should be used. This should have a clean, folded towel pinned closely about it, and permitted to extend about an inch below the lower margin of the cone. The open end of the cone should always be allowed to remain free and unobstructed. If the child is very much reduced from prolonged disease, and the operation is apt to be a long and dangerous one, the child's body should be swathed in cotton-batting or an electrotherm used on the operating table. Elmer (Archives of Pediatrics, June, 1905).

The mask used by the author is of the Allis type and dimensions, improvised from sulphite fiber covered with zinc oxide plaster, and has the Allis face-piece of rubber and a floor of wire on which are placed some layers of gauze. Within the mask is placed a 16 candle-power incandescent globe covered with several layers of gauze. The top of the mask is covered with dentist's rubber-dam tissue, in which is cut an opening about the size of a silver quarter. The anesthesia is begun with chloroform. The current is turned on with the mask about three inches from the patient's face. The drop method is used and continued until the patient acknowledges sleepiness, which is usually in from three to five minutes; then ether is substituted for the chloroform. The ether can is merely punctured with the point of a needle and the ether is forced out by the heat of the hand and sprayed on the gauze over the light, whose heat so rapidly volatilizes the ether that, in from three to seven minutes more, operative anesthesia is secured without any struggling, sense of suffocation or hypersecretion. The advantages of the method are: (1) lessened amount of anesthetic; (2) absence of the danger of ether pneumonia due to the chilling of the lung tissue; (3) absence of kidney complications because of the very small quantity of anesthetic to be eliminated; (4) almost total absence of postoperative nausea and vomiting. McRoberts (N. W. Lancet, Aug. 15, 1909).

After a small quantity of ether has been poured upon the gauze, it or the mask covered by it should be held at first some distance above the patient's face, and only gradually brought in contact. Ether vapor, being heavier than air, tends rapidly to sink into the patient's nose and mouth and by its irritating properties is therefore likely to cause, especially at first, gagging, respiratory arrest and marked subjective discomfort. By gradual approach of the mask to the face, time is allowed for the mucous membranes to become accustomed to and partly anesthetized by the vapor, whence the irritation is no longer felt and discomfort ceases. After this tolerance has become established the agent may be pushed somewhat more rapidly, though it is only occasionally advisable to make the ether vapor more concentrated than the average required to induce anesthesia in the customary period of ten or twelve minutes, as any excess over this concentration is likely to harm the mucous membranes and predispose to subsequent complications. To attempt to accelerate anesthesia by limiting the supply of air is a still more unwise procedure.

The writer deprecates the use of chloroform as an anesthetic in short operations upon the throat and nose, referring to 50 recent cases in which death had occurred in these otherwise simple operations. For infants less than 12 months old ether should be employed on an open mask. Children from 1 to 4 years of age do not take nitrous oxide well, especially if there is any obstruction of the respiratory tract. Ether in these cases is usually taken without trouble. J. H. Chaldecott (Lancet, Sept. 13, 1902).

Following plan advised for the administration of ether: The ordinary Esmarch or chloroform mask, covered with six or eight layers of gauze, is held three or four inches above the patient's mouth and nose. The patient is directed to count slowly after the anesthetist, or to breathe in and out, or to blow the vapors away. The ether contained in the ordinary chloroform bottle with dropper is allowed to drop on the mask somewhat more rapidly than if it were chloroform. The bottle is moved continuously, so that each drop falls on a different spot on the mask, and is freely mixed with air.

The mask is lowered gradually; at the same time the drops of ether are increased until a very fine, continuous, steady stream is being spread over the entire mask. The mask is finally lowered until it almost touches the face. The average patient will be able to count from 70 to 80, some only 40 or 50, while others may count 120 before unconsciousness begins. This will require from two to three minutes. At the end of a period of from five to seven minutes the patient relaxes and becomes sufficiently unconscious so that the final preparations for the operation may be begun. By the time these are completed the patient is in a condition of surgical anesthesia. To accomplish this from 2 to 2½ ounces of ether have been administered, and from twelve to fifteen minutes have elapsed. A less quantity of ether is then given.

During an operation lasting from one to one and one-half hours from 5 to 7 ounces of ether are administered. Soon after the anesthetic is discontinued the patient comes to, and frequently awakens before leaving the operating room. Metzenbaum (Jour. Amer. Med. Assoc., Nov. 17, 1906).

The average patient in the author's experience was ten minutes becoming anesthetized, and it required 2½ ounces (75 c.c.) of ether to obtain this condition. The average length of time of the operation was one hour and a quarter, and it required 5½ ounces (165 c.c.) for this time, or, in other words, about 6 ounces (180 c.c.) were used during the first hour, and about 3 ounces (90 c.c.) for the second hour.

In the treatment of accidents most dependence may be placed upon inhalations of **ammonia** and **oxygen**. H. L. Springer (N. Y. Med. Jour., June 13, 1908).

When employing the open method, the authors place a ring-shaped pad around the nose and mouth of the patient, and upon this place the inhaler. Thus the patient cannot inspire or expire air laterally. Hewitt and Symes (Lancet, Jan. 27, 1912).

The "drop method" of administering anesthetics, introduced by Witzel, consists essentially in placing the ether or chloroform on the mask in a steady, periodic, drip rather than in larger amounts at longer intervals, and also in carefully adjusting the dosage — *i.e.*, the frequency of the drops—to the conditions present at each moment of the anesthesia. The term is often applied indiscriminately to the "open method" in general, and is conducted, at least in the beginning, with the simple means already referred to, viz., a mask covered with gauze, or gauze alone. J. W. Kennedy carries out the ether "drop" procedure with a gauze towel, one yard square, which is folded into a pad nine inches square and placed in the form of a tent over the patient's face. The thumb and index-finger control the gauze, while the rest of the hand splints the lower jaw to the upper. After allowing the patient a few breaths of air, the anesthetist begins dropping the ether, and continues to drop it without intermission until surgical anesthesia is reached. If the induction is properly carried out, according to Kennedy, there is no stage of excitement and anesthesia is rapid. Where the patient coughs or struggles in the first stage, the quantity of ether should be temporarily diminished, but if the excitement characteristic of the second stage appears, the anesthetic should be dropped on more rapidly. S. G. Davis, who uses an inhaler covered with only 6 layers of gauze, advises that about the time when the patient will no longer respond to questions, a moist towel or some additional gauze be wrapped snugly around the base of the mask. The patient becomes unconscious in two or three minutes and is ready for operation in about ten minutes.

The author administered ether 337 times by the open drop method. The average time of inducing anesthesia was six minutes and ten seconds. The time varied from forty seconds to twelve minutes. Initial vomiting did not occur in a single case. In 65 per cent. of the cases there was no struggling or choking; in the remaining 35 per cent. excitement and choking occurred in a mild degree. No patient needed stimulation. Forty-eight per cent. had no nausea or vomiting following the administration ; 40 per cent. were slightly nauseated. There was no postoperative pneumonia in any case. Nephritis occurred in the case of 3 patients; 1 was a woman suffering from melancholia, which developed during pregnancy; the second was a patient suffering from appendicitis of ten weeks' standing; the third was a woman with a large uterine fibromyoma. In all 3 the physical condition was extremely poor. Shipp (Lancet, April 14, 1906).

The author describes a modified method of drop etherization. A square pad of gauze twelve layers thick, large enough to cover the patient's mouth and nose, extending well down over his cheeks, is laid directly on the patient's face. Ether is then dropped on by means of an ordinary bottle with a small wick inserted through a slit in the cork. Ether having been dropped slowly for about one minute on the pad of gauze described above, another similar pad is laid on, and the rapidity of the drops is increased and continued until the patient becomes thoroughly anesthetized. It is very important that the ether be gradually administered. The method is less disagreeable to the patient and does not cause suffocation. Postoperative vomiting is reduced from nearly 100 to 32.5 per cent. There is quicker recovery of consciousness, and there is reduction of postoperative acetonuria from 88.5 to 26 per cent. Ladd and Osgood (Annals of Surg., Sept., 1907).

For dropping ether the author suggests cutting through the soft metal cap of the ether can about four-fifths round, so that the cap can be bent back without fracture. A small pledget of absorbent cotton shaped to a wick is then inserted, and the flap turned down on it, thus forming a dropper. After use, the flap can be turned back and a cork inserted in the can. Lumbard (Med. Record, Oct. 24, 1908).

The open or drop method permits of normal oxygenation and avoids contamination of the inspired air, affords a fairly uniform ether vapor with very little distress to the patient, favors muscular relaxation, avoids exaggerated abdominal breathing, is simpler for the inexperienced anesthetist, and its safety has been demonstrated by extensive usage. On the other hand, it produces great refrigeration, gives an incomplete diffusion of ether vapor and air, requires large amounts of ether, and is slower in inducing anesthesia. The semiopen method is such as to permit of a limited amount of rebreathing. It is attained by the use of extra layers of gauze or gauze surrounded by towels, by the use of a cone containing gauze, but with both ends open, or by any one of the several inhalers arranged for limiting the air supply. Cunningham and Anderson (Jour. Amer. Med. Assoc., Nov. 7, 1908).

Experiments upon lower animals with the different methods of giving ether. Ether administered with an atmosphere of oxygen caused bronchial symptoms and some bronchorrhea, which, however, rapidly disappeared. The drop method produced slight changes in the bronchial epithelium and parenchyma of the lungs, but the alveolar epithelium was unchanged. The damaged epithelium recovered in a few days. When dangerous after-effects are produced they are due to the use of too concentrated vapor. Offergeld (Lancet, Dec. 26, 1908).

Tonsil and **adenoid operations** in children and young persons under 18 should practically always be done under a general anesthetic; over that age, when the patient has sufficient self-control and can co-operate, the author prefers local anesthesia with cocaine. The best method of giving ether or chloroform is the "drop method" on gauze, except in patients who require prolongation of the anesthesia, when the author has the anesthetist change to the vapor method, passing the ether through warm water in a wash bottle by means of a bulb compression apparatus. He always operates with the patient in the dorsal decubitus, with the head somewhat dropped over the end of the table. The upright position adds greatly to the danger of ether and chloroform. As for the anesthetic, the author decidedly prefers ether. F. R. Packard (Jour. Amer. Med. Assoc., Aug. 28, 1909).

Ether by the drop method may be given to a patient at any age. The author has administered it successfully to a patient 3 days old, and to one of 98 years. Samuel Johnston (Can. Pract. and News, March, 1912).

The signs indicating that the patient is ready for operation include contraction and immobility of the pupils, relaxation of the muscles of the jaw, and abolition of the corneal reflex.

The best way to determine if the patient is sufficiently anesthetized is by raising an arm and determining whether it is still rigid or not. The author does not believe in using the eyes as a test at this stage of the anesthetization, for if the patient is resting quietly, but still not yet completely under the influence of the ether, it is likely to excite resistance.

Having found the patient to be relaxed, the gauze may be removed from the eyes and an attempt made to see if the patient resists the opening of the eyelids, or if the eyes still twitch, as is noticed in nystagmus. One should never touch the conjunctiva to determine if the patient is under the influence of ether.

When the patient interrupts the deep natural breathing with a heavy sigh, this is a positive sign that more ether is needed. If this warning be not heeded, rigidity will soon set in, interfering with the work of the operator. H. S. Wieder (Therap. Gaz., Dec., 1907).

When the anesthesia is deep enough to suspend the swallowing reaction to salivation, the right moment is at hand for the operation to begin. J. Landström (Zentralbl. f. Chir., Oct. 30, 1909).

The true test of what may be called artistic anesthetizing is to be found in the rapidity with which the patients regain semiconsciousness after the operation. If the anesthetist is able to detect and maintain, even for a lengthy administration, an almost indistinguishable degree of lid-closure when the cornea is lightly touched, this speedy recovery will take place. F. W. Hewitt (Lancet, March 5, 1910).

The muscles of the jaw seem to feel the effect of the anesthetic before any others. The cessation of the contraction in the masseter is a much more reliable index than the sensory signs and changes in the reflexes, as this relaxation indicates that the muscles in the field of operation are likewise relaxing, which is not always the case when only the reflexes are abolished. Fiori (Policlinico, March 13, 1910).

The *"closed method"* of inducing anesthesia involves nowadays the use of more cumbersome and expensive inhalers such as those of Clover, Bennett, Hewitt, Ormsby, Gwathmey, Junker and Vernon Harcourt (the last two for chloroform mainly). Clover's apparatus (Fig. 3)—as well as the three mentioned after it—consist of a bag, a receptacle for ether, a mixing chamber, and a closely fitting mouthpiece with an inflatable rubber rim. With these inhalers the patient breathes immediately into and out of the bag, though openings for the entrance of fresh air are also provided. A regulating mechanism is supplied by which, after beginning with pure air, the patient can be made to breathe gradually increasing amounts of ether, the concentration of the vapor being mechanically under control and constantly adjustable to the desired percentage.

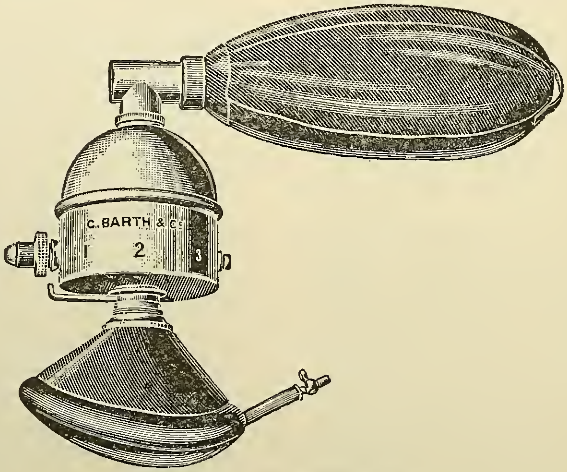

Fig. 3.—Clover's ether inhaler.

Where untoward symptoms, stertorous respiration or cyanosis, appear, the face-piece is lifted off and fresh air admitted, or, sometimes, a breath of fresh air is allowed periodically after a given number of respirations in the inhaler. With these inhalers the ether vapor is warmed by the patient's expired air. A disadvantage, on the other hand, is that, in general, partial asphyxia is a factor in the anesthesia as well as the ether—an unfavorable circumstance during operations on enfeebled subjects.

The Junker inhaler (Fig. 4) as modified by Krohne consists of a vulcanite face-piece, connected by rubber tubing with a cylindrical graduated container for the anesthetic, this in turn being connected with a pair of rubber bulbs, by which air is blown through the anesthetic and then out into the face-piece. The Junker apparatus has been widely used, but is disadvantageous in that the closed mask is not sufficiently large to hold vapor for a full inspiration, and unnecessary work is thus thrown on both the respiratory and circulatory centers (Gwathmey). This danger can be overcome by attaching a thin rubber bag, to be constantly two-thirds inflated with air, just behind the inhaler.

The same objection has been raised to the Harcourt inhaler (Fig. 5). This apparatus, moreover, is intended solely for use with chloroform, of which it supplies a vapor of accurately gauged concentration.

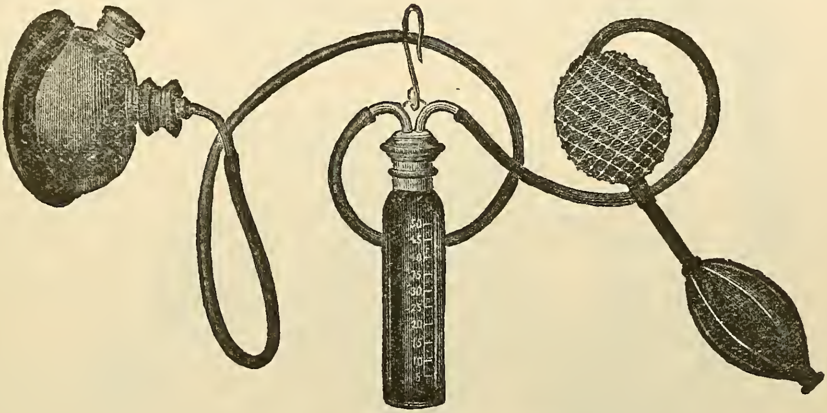

Fig. 4.—The Junker apparatus. (Medical Record.)

Gwathmey's apparatus for "vapor anesthesia" (Fig. 6) consists of a face-piece resembling an Esmarch mask but having a hollow rim, which is perforated with small holes to allow the vapor from the apparatus proper to escape under the mask and be respired by the patient. This mask is covered with 2 to 4 layers of gauze, over which is placed oiled silk or rubber tissue, provided with a central opening the size of a dime, so that during the period of induction a few drops of **chloroform** may be added, if necessary, in vigorous alcoholics. There are no valves in the apparatus, and therefore no rebreathing nor strained breathing at any time. In each of the three six-ounce bottles there are four tubes, varying in length from one that reaches to the bottom of the bottle to one that only penetrates the stopper. These tubes represent four different degrees of vapor strength. The percentage of the vapor varies according to the depth and temperature of the fluid in the bottles, the size of the hand-bulb, and the pressure with which the air or oxygen is forced through the tubes, either by the bulb or from an oxygen tank. There is no possibility of the patient's getting a vapor of dangerously high concentration. One can give either a pure chloroform or ether vapor, or any combination of them, varying in intensity as circumstances require. In an emergency, oxygen can be given without disturbing the inhaler or the mask. Weak, anemic men, and the majority of women, can be anesthetized with the ether vapor alone. Changes from one narcotic to the other are done by simply turning a lever.

In the third bottle of the Gwathmey apparatus is placed, to render the induction stage pleasant, for a woman her favorite cologne, and for a man a highball or something similar. **Oil of orange** may also be used.

The anesthetic is started with a 1 per cent. vapor of cologne or whisky, and, as soon as the mucous membranes have become accustomed to this, a fractional per cent. vapor of chloroform is added for the first minute. This is changed gradually, but as rapidly as possible, so that at the end of three minutes the patient is getting 1 per cent. vapor of chloroform and a fractional per cent. of cologne or highball, after which the latter is turned off entirely. The average time to induce surgical anesthesia is six minutes. The third bottle is then taken out, emptied, and refilled with hot water at about 100° F. (37.8° C.). When the chloroform or ether vapor is passed through this hot water, it is raised to the temperature of the blood, making it safer as regards life, and also more respirable, and still further reducing the after-effects. Or the cologne can be sprinkled on the mask, and hot water used from the first in the third bottle.

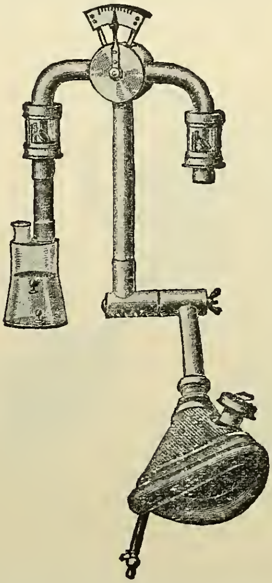

Fig. 5.—The Harcourt inhaler. (Medical Record.)

A very satisfactory method is to use the gas-ether sequence as a preliminary, and then allow the reflexes to become active, when oxygen-chloroform vapor is begun. Another method is to commence with gas, then change to the vapor mask upon which 10 c.c. (2½ drams) of ethyl chloride has been poured, and continue with the chloroform vapor and air. After the operation has commenced, oxygen instead of air is allowed to flow through the chloroform. Still another method is to dispense with the gas and commence with the vapor mask, using ethyl chloride at the start.

An advantage of the vapor method of anesthesia is the fact that excitement is usually absent, or very slight. In the surgical stage the patient's breathing is regular and natural. The lid reflex is never entirely abolished, nor is there stertor or snoring or the mucous râle, even when giving pure ether. There is complete relaxation without the slow pulse of chloroform (as usually administered), or the billowy breathing and rapid, bounding pulse of ether. The total amount of anesthetic used is remarkably small. In the majority of cases there is absence of unpleasant after-effects. A continual narcosis is maintained without any danger to the patient.

Oxygen should be used whenever possible, especially with chloroform, as it has been proven that this combination is safer than ether and air. The author always uses chloroform and oxygen whenever and as long as possible, and continues the anesthesia with ether whenever this is indicated. The usual precaution of not giving ether in the presence of an open flame applies with double force to the more explosive mixture. The change from air to oxygen should not be made usually until the patient is well under the anesthetic and the operation has begun. J. T. Gwathmey (Med. Record, Oct. 14, 1905).

Description of an apparatus for narcosis under plus pressure. The apparatus is designed to allow the anesthetist to sit in the cabinet into which the head of the subject projects. This leaves the operator and his assistants free to operate under normal conditions, with access to instruments, etc. The large box or chamber is made light and movable, and the ventilation is so contrived that the fumes of the anesthetic are conducted away without reaching the anesthetist. The other modes of applying narcosis under plus pressure that have been suggested are the use of a diver's helmet for the subject, or of a mask which closes mouth and nose airtight, or Kuhn's intubation, or tracheotomy. Engelken (Deut. med. Woch., Dec. 15, 1904).

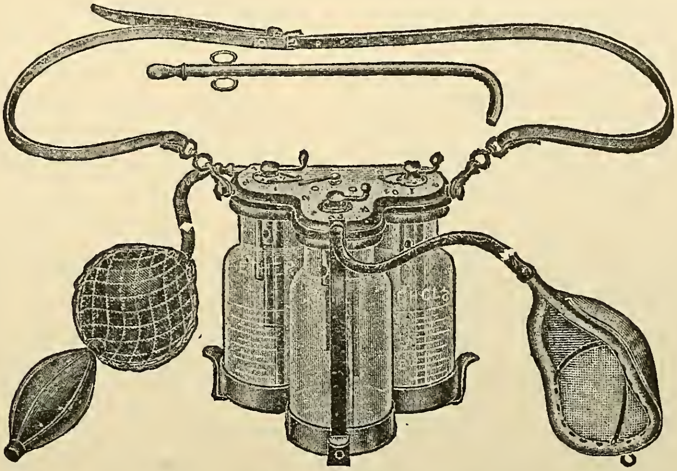
Fig. 6.—The Gwathmey vapor inhaler. (Medical Record.)

General Management of Ether Narcosis.—An important feature in anesthesia is the management of the patient's jaw. It should be kept constantly forward, and this may be accomplished by placing the thumb on the malar prominence and exerting pressure from behind forward with the middle or ring finger under the angle of the jaw. As the muscles relax, the lower teeth may be hooked in front of the upper. At the same time the head should be rotated to one side and slightly extended—a position which removes the effect of gravity on the jaw and facilitates the passage of air through the larynx. One finger may be used to palpate the facial artery as it curves round the inferior border of the jawbone, and thus keep track of the pulse rate and volume; a mouth-gag and tongue forceps are seldom required when the jaw is correctly managed (Mellish).

The following method suggested as substitute for the painful mouth-gag and tongue forceps: With the head low, after opening the mouth with the gag, a broad, round, gauze pad, 3 to 4 cm. thick, held on a handle, is introduced on the side of the mouth opposite the gag. The introduction should be made with a rotating movement, so that the tongue is lifted forward. The pad is then rolled on the surface of the tongue until it rests on the base in front of the epiglottis, when the tongue will be resting on it. By drawing it in the direction of the submental region the tongue is lifted forward. The epiglottis follows this movement, and the larynx is kept open. It is easy to hold the instrument in this way during the whole operation, but this is rendered still easier by resting the shaft of the handle on the upper teeth. Since the pad gradually becomes saturated with mucus, it must be changed at times. When the pad and handle are in, the mouth-gag is not necessary and is removed. Gonterman (Zentralbl. f. Chir., Bd. xxxviii, S. 1626, 1911).

When surgical anesthesia has been secured, the amount of anesthetic used should invariably be reduced, and, in fact, the aim throughout should be to administer as little of the drug as is compatible with the operative requirements.

> During the opening of the abdomen and the walling off of the intestines full anesthesia is usually best. As soon as the operation proper is begun, the drug may be much diminished or even withdrawn for a time. During the closure of the peritoneum the amount may have to be increased, but the mask may usually be taken away after this and the rest of the incision closed without it. One likes to see a patient moving during the latter part of this process and talk while he is yet on the table. R. R. Smith (Phys. and Surg., March, 1910).

> Very little of any anesthetic is needed to keep up any level of narcosis when the level is once established. When a narcosis is maintained without excessive interaction between the narcotizing agent and the tissues of the body, such tissues, even if temporarily damaged, will rapidly recover, provided their requirements—*e.g.*, adequate blood-supply—are safeguarded. D. W. Buxton (Lancet, May 11, 1912).

Where retching and vomiting occur during anesthesia, the patient's head should be tilted to one side, if it is not already in this position, in order to cause the regurgitated fluid—chiefly mucus and saliva—to recede from the air-passages. The mouth should be opened with the gag, if necessary, and the liquids present in it swabbed out with gauze sponges held in forceps. The vomiting is of no importance in itself, but is of great significance if the freedom of the air-passages is not constantly borne in mind, since aspiration of some of the ejected material may cause asphyxia. When the mouth has been opened and cleared, it is well to draw out the tongue with the fingers (protected by a napkin or gauze) so as to facilitate the passage of air through the larynx by raising the epiglottis; or the index finger may be passed into the mouth back to the epiglottis, and the latter, together with the tongue, directly lifted forward.

If any degree of asphyxia shows itself, **Laborde's method** of stimulating respiration — traction on the tongue rhythmically, 15 or 18 times a minute—may be practised.

> Excessive traction should not be exerted upon the tongue, for Crile has shown experimentally that this in itself is sufficient to cause a cessation of respiration, with fall of blood-pressure, etc. H. S. Wieder (Therap. Gaz., Dec., 1907).

Vomiting unattended by other untoward symptoms does not preclude continuation of the ether.

Embarrassed or arrested respiration, as well as marked excitement, in the earlier stages of anesthesia are best treated by temporary withdrawal of the anesthetic.

The question of proper regulation of the dosage of ether administered is one that must be continually before the anesthetist's mind, and is of paramount importance to the patient's interests. Contraction and immobility of the pupil constitute the chief sign that the proper degree of anesthesia is being maintained. Dilatation, then, signifies either that there is danger or that too little ether is being given. But in cases where pupillary contraction does not occur, other indications have to be watched for, in particular those relating to the respiration, circulation, and color of the skin. Insufficient anesthesia is suggested usually by quickened breathing, together with good skin coloration and circulatory activity. According to F. E. Simpson, the most valuable sign of beginning awakening of the patient is a lateral rolling of the eyeball from side to side, which precedes by some moments other evidences of returning consciousness. The rotation is slow and hesitating, and recurs at intervals of a few seconds; it signifies to the anesthetist that by adding a few drops more of ether from time to time he can prolong the proper operative condition for an almost indefinite period.

On the other hand, a suddenly dilating and subsequently immobile pupil, lividity of the face, and perhaps a pronounced increase in the pulse rate—from 90 to 120 or more—with diminution of the pulse volume and slowing and jerkiness of the respiration, indicate that the danger stage of anesthesia has been reached and greater caution in dosage is necessary. Cyanosis is frequently due merely to an insufficient allowance of air, which can readily be corrected, and is therefore less ominous than pallor, which tends to show, on the other hand, that circulatory activity is being gradually undermined by the drug.

> There is a much greater interval of safety between the corneal reflex and the failure of respiration and heart than is generally admitted. Further, the reaction to corneal stimulation varies enormously in different individuals. The corneal reflex cannot be depended upon as a guide in the administration of anesthetics in cases requiring complete muscular relaxation, especially in abdominal and hemorrhoidal operations; in these, moderate secondary dilatation of the pupil, while keeping a careful watch on the respiration and pulse, is the best guide. Gardner (Brit. Med. Jour., April 22, 1900).
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> The conjunctival reflex is of little value in the majority of deeply etherized patients. The exceptional cases in which it persists are alcoholics and those with a full, hard pulse, as in chronic nephritis. The pupil reflex, however, is of great value in ether administration. The pupil of simple ether anesthesia is usually moderately dilated and round; it shows no immediate reaction to light, but if it be kept exposed, without further administration, it gradually contracts with jerky movements generally synchronous with the inspirations. In strong, muscular men; in those of either sex with hard pulses, alcoholics, and where **morphine** has been previously administered, the pupil approaches rather to the chloroform type. In deep etherization the pupil gradually enlarges till it is widely dilated, immobile, and usually irregular in outline. With this pupil in ether anesthesia there is a quiet, regular pulse and equally satisfactory respiration, and if the ether be withdrawn the pupils gradually contract to the moderately dilated, regularly outlined condition; the pulse and respiration continuing unaltered or but slightly accelerated. If administration be now not recontinued, there will eventually come a deep, sighing inspiration, which the author considers the best indication of all for more anesthetic. If it be not given the pupils continue to contract to the condition found in deep sleep, unless emesis occurs, when they become dilated.
>
> One of the causes of the larger pupils in ether anesthesia as compared with chloroform anesthesia is the greater intraocular tension, due to the higher blood-pressure. A similar dilatation is temporarily caused by undue pressure over the cornea in ill-advised attempts to elicit a corneal reflex. Any but the gentlest touching of the conjunctiva is apt not only to damage the epithelium, but also quickly renders it less sensitive, and so diminishes the use of the test. Lawkins (Austral. Med. Gaz., Jan. 20, 1903).

The diagnosis between pure respiratory and pure circulatory cyanosis is easily made by noting the capillary circulation. This is most readily done by compressing the finger-nails and noting the more or less rapid return of the expelled blood. Pedersen (Med. News, Dec. 31, 1904).

It is impossible under any known conditions for the respiratory center or the cardiac center to be poisoned by chloroform or ether while the upper eyelid still closes when the center of the cornea is touched by the finger. The administrator, standing behind the patient, inserts the pulp of his middle finger between the palpebral edges, drawing the upper eyelid upward and at the same time brushing that finger-pulp lightly against the center of the cornea. When he has arrived at the upper limit of the pupil he should let go altogether, noting both by the senses of touch and sight the degree of briskness with which that upper eyelid closes. When a definite difference exists in the activity of the two upper eyelids, one must be guided by the more active.

Pupillary signs may be neglected altogether. A progressive dose of chloroform or ether having been given until the upper eyelid is weakly active in response to corneal contact, this condition can be exactly retained throughout by stopping the anesthetic for a few breaths to quicken its activity, or giving more anesthetic to weaken it as required. As to the air-ways, it is necessary to know by the sound of the breathing when they are clear. Every expiration must be either heard or felt, to make sure that efficient breathing is going on. It is of no use to see the abdominal and thoracic movements, for they may proceed for a considerable time after obstruction to air entry has taken place. Duskiness of the lips and ears is a sign that air is not entering the lungs in adequate amount. The administrator should put in a small mouth-prop, raise the jaw or draw the tongue forward, directly the sound of breathing through clear air-ways is replaced by that of partially obstructed respiration. Gardner (Brit. Med. Jour., June 5, 1909).

A stertorous respiration suggests either an excess of anesthetic or an obstruction to breathing, such as mucus, falling back of the tongue, or laryngeal edema. That one of the latter causes is active can usually be determined without difficulty upon investigation. Holding the jaw well forward, as already described, and drawing on the tongue, are useful diagnostic procedures in this connection. The anesthetist should bear in mind that visible respiratory movements of the chest do not necessarily certify to the entrance of air into the lungs, and should therefore be on the alert for any indication of respiratory difficulty; otherwise, the patient may be unwittingly allowed to pass into a condition of serious respiratory depression.

There are many ways in which the respiratory passage may be obstructed. A large thyroid may press on the trachea till respiration is difficult when the patient is conscious, and insufficient when ether is given.

Vigorous efforts on the part of the surgeon removing an enlarged thyroid or glands of the neck may cause cessation of respiration, either from constriction of the trachea or possibly through vagus inhibition.

The risk of giving ether to persons suffering from cellulitis of the neck should always be remembered, for in severe cases of this kind there is generally coexistent edema of the larynx, which may be increased by the effect of ether till it produces asphyxia. Even then, when laryngotomy is performed quickly, the patient's life will generally be saved.

Asphyxia may be caused by the inspiration of vomited matter, most frequently in cases of intestinal obstruction in which the vomiting is almost continuous, and in large quantities. By keeping a pillow under one shoulder, however, the vomit may generally be made to run out of the mouth. R. J. Probyn-Williams (Clinical Jour., Dec. 23, 1908).

Case of nitrous oxide-ether anesthesia complicated by bronchorrhea. The pulse increased in rapidity and lost volume, the respirations became shallow and irregular, and the patient cyanotic. The moment the ether was withheld the patient promptly offered resistance, and when more was administered his breathing was interfered with. The author ordered a 5 per cent. solution of **epinephrin** 1: 1000, diluted 1 to 20, and with this mopped out the pharynx. Almost immediately the secretion of mucus became less, the respirations clearer and deeper, and the patient less cyanotic. The author then used epinephrin in anesthesia as a routine in a series of cases. He found that a 25 per cent. aqueous solution of the standard 1: 1000 gave the best results. Pouring ether in the towel cone and spraying the epinephrin solution on it, depending on the ether to vaporize it sufficiently for inhalation, is the best mode of administration. Three- to six- minute intervals are sufficient for its use, and a total of from ½ to 1 ounce of this solution is enough for an operation lasting from thirty minutes to an hour. The effects are a more uniform etherization, the pulse becoming steadier and slower. The respirations are quiet and regular, and the bronchial secretions are practically checked. Recovery from the anesthetic was uniformly good.

The epinephrin, acting generally from absorption, is a powerful stimulant; it materially lessens shock, lessens the capillary ooze at the field of operation, and is of great benefit to the much weakened patient. Venable (Va. Med. Mthly., Feb. 22, 1907).

Within a reasonable limit, quality, not rate, is the consideration in observing the pulse; and depth, not rate, of the respiration. As to the pupil, one should use it more as an arbiter when it is necessary to decide between two seemingly opposed factors, or to decide the importance, when otherwise all seems well, of the presence of certain conditions, as cyanosis, stertor, continued rigidity, or an increasing rapidity of pulse, or shallowness of respiration.

The presence throughout anesthesia of stertor or a slight degree of cyanosis need not alarm unduly, but should cause increased watchfulness, since its presence is always indicative of obstruction to the passage of air, though such interference may be exceedingly slight. Many of the more plethoric exhibit cyanosis from the induction and throughout the anesthesia without apparent significance, but in the arteriosclerotic cyanosis is apt to be the precursor of danger.

Respiration simply rapid, say 30 or 40, need seldom be viewed with gravity, but not so any irregularity or rhythm or extreme shallowness. Preceding the return of reflexes with accompanying vomiting there may be an apparently unexplainable change for the worse in the pulse. It is in such cases that reference to the eye is of much value.

Laryngeal spasm may be avoided or be generally overcome without difficulty in the initial stage by the free admission of air. But the occurrence and recurrence of this spasm during deeper anesthesia may be prophetic of trouble. In such, air should not be restricted and ether very cautiously given. If the free admission of air does not overcome the spasm, the jaws should be pried apart and the tongue forcibly drawn forward. J. B. Bogan (N. Y. Med. Jour., Sept. 24, 1910).

It is neither wise nor necessary to obtain a degree of anesthesia free from all reflex movements of the thighs for **circumcision** in childhood; but, having weakened the corneal reflex, it is well to get the nurse to place her hand on the patient's knees to prevent their upward reflex movement when the prepuce is first seized. Reflex laryngeal crowing almost always arises also at this moment, and the lips should then be rubbed briskly with a towel to stimulate deeper breathing; the jaw should be pushed forward and the anesthetic withheld until respiration is more regular. In operations for **adenoids** and **enlarged tonsils** it must be borne in mind that patients with these affections have more or less obstructed air-passages, and that the operation and the bleeding it causes also cause intermittent respiratory obstruction. Gardner (Brit. Med. Jour., June 5, 1909).

In chronic alcoholic or nervous patients, considerable difficulty is not infrequently experienced in inducing proper anesthesia. In such cases the cautious administration of chloroform for a short time will often prove effectual. In "florid" individuals in general, a fairly deep anesthesia is usually to be maintained, in order to avoid troublesome reflex manifestations. In obese subjects it is particularly necessary that there be no insufficiency of air-supply; hence the "closed" methods of ether administration are by many considered inadvisable for such patients. The anesthetist should remember that after the breathing has temporarily ceased owing to reflex irritation, or when in the operation sensitive or inflamed tissues are being dealt with or the anal sphincter is being stretched, deep respirations occur which tend to increase suddenly and markedly the amount of ether taken into the patient's lungs. Some degree of caution as to the quantity of ether supplied under such circumstances is therefore required.

Muscularity often causes delay and difficulty in anesthetization, and as a large number of fatalities from chloroform have occurred in patients of this type, ether should be chosen wherever possible rather than chloroform. Generally, a mixture of **chloroform** and ether, administered slowly, gives better results than ether or chloroform in muscular and obese subjects. Patients confined to bed for a considerable time owing to some constitutional disease are not, as a rule, bad subjects for anesthesia. Hewitt (Lancet, Jan. 10 and 17, 1903).

Patients meeting with an accident causing dislocation of a limb are unprepared by abstinence from food for an anesthetic, and are not likely to take it well. A jaw-gag must be at hand in case of semisolid vomiting, and whatever anesthetic is used to make the patient unconscious, ether should afterward be given to obtain muscular relaxation. A great many deaths have occurred under chloroform unwisely pushed for this purpose. **C. E.** followed by ether or gas and ether are the most valuable and safe anesthetics to employ. Gardner (Brit. Med. Jour., June 5, 1909).

The **nitrous oxide** and **oxygen-ether-chloroform** sequence may be employed to eliminate the dangerous induction period of chloroform anesthesia when it is desirable to employ that anesthetic. W. H. Allen (Jour. Amer. Med. Assoc., Nov. 11, 1911).

The fact that ether is easily ignited should always be borne in mind.

The writer reports the following unusual experience: While engaged in a tedious and difficult operation, his attention was taken from his work by a sudden flash of light and some quick movements on the part of the anesthetist. The ether vapor had ignited, scorching the hair and eyebrows of the patient, and had burned the skin on his forehead sufficiently to cause quite a marked redness. The anesthetist reported that the patient being on the face, he was unable to see the pupil properly, and he had turned on the electric light in order that he might more readily note the reaction of the pupil. The blaze had occurred coincidently with the turning on of the light. There was no exposed fire in any part of the operating room, and the only conclusion was that the vapor of ether had ignited from the spark in the electric light burner made when contact took place in turning on the light.

It is well for any surgeon or anesthetist not to turn electric lights on or off near ether vapor, particularly when the room is small and there is a large amount of the vapor in it. Yet it is not so easy to produce a blaze by the turning on of an electric light in the presence of ether when one tries it for that purpose. Since the above occurrence, the author has tried the experiment several different times in different ways, with the same burner and others, and has been unable to produce a blaze with ether vapor. Thus, while it is possible that this experience may be unique, and it is certainly of rare occurrence, every surgeon and anesthetist should bear in mind the fact that it has occurred. Very serious consequences might easily have resulted in this case if the anesthetist had lost his head. D. H. Murray (N. Y. Med. Jour., June 27, 1903).

Postanesthetic Precautions.—After the patient is removed from the warm operating room, it is of the greatest importance that he be protected from cold and draughts of air while being removed to bed. The bedroom and the bed should be warm. Aspiration pneumonia should be guarded against by seeing that the patient does not unnecessarily inspire vomited material into the trachea. The system should be amply supplied with fluids, either by stomach, by rectum or subcutaneously, in the form of normal saline solution, and as much nourishment should be given as conditions permit (Mellish). The suggestion has been made that the patient be required, wherever possible, to breathe deeply for a period after the anesthesia, in order to hasten the elimination of the drug from the system and minimize any harmful effects to which prolonged contact of it with the visceral parenchymas may give rise.

Proper care during the first twelve hours after anesthesia is equally as important as the administration itself. The average patient should be able to talk coherently thirteen minutes after the anesthetic has been discontinued. It is best, if the pathological conditions permit, to put the patient on his side immediately after operation. This allows the tongue to drop forward and keeps the throat free. **Copious drafts of hot water** should be given, to avoid dry retching, and at the same time wash out the stomach if the patient vomits. The patient should be heavily covered, to encourage perspiration and render less likely congestion of the lungs and kidneys. Pedersen (Med. News, Dec. 31, 1904).

The writer places his patients in a sitting posture immediately the operation is finished, no matter what the condition operated for, and almost never witnesses vomiting or nausea. He ascribes this to the avoidance of congestion in the medulla and also to the fact that pressure of the abdominal viscera is removed from the diaphragm by gravity. Chandler (Surg., Gynec., and Obstet., Nov., 1911).

Following points relating to anesthesia emphasized: Never use alcohol as a stimulant during or after an anesthesia if the opsonic power of the blood is of any importance. Make the anesthesia as short as possible. Take special precautions for asepsis and antisepsis in all operations of any length. A very slight infection, which would not manifest itself under ordinary circumstances, may develop into a serious condition after an anesthesia because of the impaired resistance. Inject slowly 6 ounces (180 c.c.) of pure limpid **olive oil** high up into the rectum in all septic cases, and in all others in which the patient's power to resist infection may be called into play. Ferguson (N. Y. Med. Jour., May 11, 1912).

UNTOWARD EFFECTS. — A. **During Anesthesia.—Respiratory arrest** may occur as a primary effect of the administration of an excess of ether. In the early stages it is due to irritation of the mucous membranes and is relieved by temporary removal of the anesthetic, supplemented, if necessary, by **artificial respiration.**

> Breathing may cease during surgical anesthesia (*a*) from the presence of muscular spasm or some other condition within the air-passages, causing occlusion; (*b*) from some external agency preventing lung expansion; (*c*) from a diminution or arrest of the blood-supply to the respiratory centers; and (*d*) from the toxic effect of the anesthetic upon those centers. A frequent cause of difficulty in inducing and maintaining anesthesia is the presence of partial or complete nasal obstruction. Whenever practicable, oral breathing should be secured and maintained in preference to nasal breathing, for the latter is often inadequate, retarding the onset of anesthesia and leading to hyperpnea, venous engorgement, and abdominal rigidity. By the most careful attention to symptoms the anesthetist may, in the great majority of cases, and particularly toward the close of operations, permit the patient to display a slight trace of corneal reflex. Hewitt (Lancet, July 20, 1907).

Later in the anesthesia, however, it is due to the direct effect of an excess of ether on the respiratory center, and is likely to be accompanied by **dilatation of the pupils,** loss of the **conjunctival** reflex, and soon after **by cyanosis** and objective evidences of secondary circulatory enfeeblement.

The *treatment* of the latter form of respiratory arrest consists in **immediate removal of the anesthetic, lowering** of the **head of the operating table,** and **artificial respiration.**

> Case of total respiratory failure from ether following an operation for appendicitis. **Artificial respiration** was practiced for over four hours, and various stimulants were also used, followed by recovery. The only agents which seemed to be of service were artificial respiration and **adrenalin chloride.** Discontinuance of artificial respiration always produced cyanosis. Renewed efforts restored the color of the skin. To the adrenalin chloride belongs the greater part of the credit of resuscitation. It lowered the beat of the heart to nearly normal and increased its power and volume. At no time after the first dose of 30 minims (1.8 c.c.) did the action of the heart fail. It was administered the day after the operation in doses of 10 drops every two hours. This drug, in the writer's experience, is the one valuable thing in cases of cardiac failure from shock and hemorrhage. H. H. Everett (Medical Record, May 23, 1903).

> **Rhythmical tractions on the neck** have exactly the same effect as the rhythmical traction on the tongue. The maneuver consists in standing behind the head of the patient and then stretching the neck backward and forward twenty or thirty times a minute. Depage (Jour. de Chir. et Annales de la Soc. Belge de Chir., Jan., 1904).

Collapse, implying primarily a weakening of the circulatory rather than the respiratory functions, is less likely to occur under ether than under chloroform. Sudden cardiac paresis and inhibition, such as can readily be produced by incautious administration of chloroform in the early stage of induction, is a comparatively rare event in the case of ether. Circulatory weakening from the latter drug more characteristically occurs after prolonged complete surgical anesthesia. The pulse is observed gradually to become feeble and irregular, dilatation and immobility of the pupils are noted, pallor or cyanosis appear, and the heart action may ultimately completely stop—synchronously with, or only slightly preceding, respiratory enfeeblement and arrest. The condition present is one of cardiac dilatation and likewise vascular dilatation, the vasomotor center being generally simultaneously impaired.

The *treatment* of collapse consists in **stopping the ether, raising the feet,** and **lowering the head**—in order to improve the blood-supply to the bulbar centers,—instituting **artificial respiration** to prevent further weakening of the heart through imperfect oxygenation and favor removal of ether from the system, and the application of various stimulant and other supporting measures. **Oxygen inhalations** should be at once instituted. **Forcible compression of the heart** with clenched fist, 120 times a minute, through the chest-wall, is likely to prove of value, where there is no abdominal opening, in emptying the overburdened heart, and may even be employed with the idea of creating an artificial carotid pulse. In abdominal operations **massage of the heart** may be practised by inserting one hand in the peritoneal cavity and rhythmically squeezing the heart through the relaxed diaphragm between the thumb and finger, or compressing it between the inserted hand and the other hand placed on the precordium externally. These compressions should be repeated 20 to 40 times a minute. Mechanical cardiac stimulation has also been effected with a finger passed through an incision in the chest wall, in the fourth intercostal space.

> A patient who had withstood one hour of chloroform-ether narcosis without trouble, suddenly went into complete collapse. Trendelenburg posture, artificial respiration, oxygen and hypodermic stimulation failed to restore. When no signs of life were obtained for five minutes subdiaphragmatic **massage of the flabby heart** was begun in combination with the other measures. After two minutes the heart grew firmer and a few cardiac and respiratory movements were noted, but when the massage was stopped complete syncope returned. The massage was resumed and the heart responded after one minute. Gradually the heart began to recover, and all the vital functions slowly returned. The patient recovered from the operation. A. T. Jurasz (Münch. med. Woch., Jan. 10, 1911).

In a large percentage of patients succumbing to primary cardiac failure under ether there has, in all probability, been no real heart disease and no status lymphaticus, but an acute susceptibility equivalent to these conditions has been developed by unskillful anesthesia. A fatality of this class seldom occurs after profound and prolonged anesthesia. It is especially the sequel of light anesthesia.

Usually the printed accounts of such cases state expressly that the administration of ether was interrupted once, or twice, or several times, thus allowing the subject to come nearly out of anesthesia. The patient may even have winked his eye only a few seconds before the circulation suddenly failed. He may have drawn deep, gasping breaths some time after the heart had completely stopped beating. Quite often the case is that of a child under operation for adenoids.

This form of death and, in fact, by far the greater number of all deaths under anesthesia are fundamentally due to acapnia resulting from the excessive pulmonary ventilation of the stage of excitement. Experimental evidence shows that acapnia exerts deleterious effects upon the heart, and upon many other functions, no less than upon respiration. Dogs which have not been excited at any stage usually take chloroform well. If one gives too much chloroform, respiration usually stops some time before the heart. If, on the contrary, the subject has first been rendered acapnic, the hypersusceptibility thus produced renders even the strongest animals liable to sudden primary cardiac failure under an otherwise moderate dosage of chloroform. Y. Henderson (Surg., Gynec., and Obstet., Aug., 1911).

Venesection has been practised to relieve engorgement of the right heart.

Other valuable measures include the intravenous injection of warm **saline solution**, to which a few to 20 drops of 1 : 1000 **epinephrin** solution are — preferably gradually — added, **bandaging of the limbs and abdomen** to compensate for vascular relaxation and improve the blood-supply to the centers and heart, and **external heat**, applied by means of hot blankets and water bottles.

Experimental research on resuscitation of dogs killed by anesthetics showed that **Ringer's solution** yields more favorable results than saline solution. The most satisfactory results were obtained with the infusion bottle at a height of five or six feet. Crile and Dolley (Jour. of Exper. Med., Dec. 21, 1907).

Drugs, such as **strychnine** (1/20 grain — 0.003 Gm.), **digitalis** (10 minims — 0.6 c.c. — of fluidextract), **atropine** (1/100 grain—0.00065 Gm.), **caffeine sodiobenzoate** (8 grains—0.5 Gm.), and **cocaine** (1/4 grain—0.016 Gm.), sometimes do not prove of immediate service in combating the circulatory depression, but are useful to maintain cardiovascular activity once it has been partially restored by other measures. Injections of sterile **camphorated oil**, 20 minims (1.25 c.c.), may be given. Alcohol is of doubtful value, and the nitrites are to be eschewed. **Rectal injection of warm coffee** constitutes a useful measure.

Shock, consisting essentially of vasomotor exhaustion, with cardiac enfeeblement, if present, only a secondary manifestation, is to be differentiated from collapse due more directly to the anesthetic. It may come on during an operation and persist after it is ended, and may be due either to overstimulation of the nervous system the result of excessive tissue injury during the operation (Crile), to hemorrhage, or to exposure to cold. The symptoms consist of pallor, sweating; a soft, irregular, and accelerated pulse (especially if there has been much hemorrhage), and respiration that is at first deep and sighing, then feeble. Shock is distinguished from the effects of an overdose of the anesthetic by the persistence of the corneal reflex, through an appreciation of the severity of the operation, and by consideration of the preceding depth and duration of anesthesia, the anesthetist judging the probable effects of the amount of anesthetic already used.

Respiratory surgical shock is most common during light or moderate anesthesia, before the corneal reflex has vanished; while circulatory shock, which is by far more common under chloroform, is met with during profound narcosis. Respiratory shock is specially liable to complicate operations upon the rectum, urethra, abdominal organs, uterus, perineum, and kidney. The immediate cause is usually a reflex spasm affecting either the tongue, fauces, palate, and adjacent parts, and having stertor as its audible expression; the larynx, and producing stridor; or the respiratory muscles, and bringing about respiratory spasm. Circulatory shock is chiefly met with in operations on parts possessing important nerves or rich in nerve-supply. The immediate cause is usually a sudden relaxation or paralysis of the vasomotor system, generally associated with some cardiac inhibition. The favorable conditions for the establishment of respiratory shock are partial anesthesia, manipulations upon sensitive parts, and the presence of an air-way likely to become occluded. Those for circulatory shock are deep chloroform anesthesia, the horizontal, semirecumbent, or sitting posture, and intestinal, omental, uterine, or renal traction. Simple chloroform overdosage may be indistinguishable from circulatory shock. Respiratory shock may usually be avoided by securing full anesthesia before the patient is moved, and by so adjusting the degree of anesthesia that reflex modifications in respiration are as far as possible eliminated. Circulatory shock can be avoided by using ether instead of chloroform; if the latter is used, too deep anesthesia must be avoided, and the patient placed in the Trendelenburg posture, in which position circulatory shock is almost never seen.

The treatment of respiratory shock is to re-establish respiration as soon as possible by separating the clenched teeth, sponging out the fauces, pushing the lower jaw forward, **tongue traction, artificial respiration,** and, if need be, **laryngotomy** and direct **lung inflation.** The treatment of mild circulatory shock is to lessen the depth of anesthesia and to substitute a chloroform-ether mixture, or ether for the chloroform. When severe, the anesthetic must be withdrawn, the **head lowered,** the **feet raised,** and **artificial respiration** be performed. Unless the patient be very deeply anesthetized recovery can be effected very rapidly, and the operation proceeded with. Drugs are of little or no value. Hewitt (Lancet, July 27, 1907).

The *treatment* involves both prophylaxis and the application of active measures when the condition has already become established.

The treatment of surgical shock and collapse should be very largely by prophylaxis. The anesthetist should give as little anesthetic as possible. In certain brain and abdominal cases the operator and the anesthetist should work together, the depth of the narcosis increasing and diminishing as indicated by the operative manipulations. The anesthetist should notify the nurse to prevent any unnecessary exposure of the body. The "nerve-blocking" procedure of Crile should be used to lessen the shock, when operating on an extremity. The large nerve-trunks are cut down on after anesthesia and are injected with 4 to 10 minims (0.25 to 0.6 c.c.) of 4 per cent. cocaine. Caswell (Boston Med. and Surg. Jour., June 28, 1906).

Wherever shock is seen to be present before operation, *e.g.,* where the patient has been severely injured in an accident, an injection of **morphine,** together with infusion of **saline solution** and **epinephrin,** will serve as prophylactic procedures.

Where shock develops during an operation, drugs such as **pituitary extract** and **digitalis** should be administered, and many of the measures already described under Collapse—**lowering** of the **head, external heat, bandaging** of the **limbs and abdomen**—brought into requisition. **Crile's pneumatic suit,** serving the same purpose as bandaging, may be used with marked advantage, if available.

Adrenalin is the only drug to be used in true surgical shock. It should be given with saline solution by intravenous infusion. The proportions of adrenalin are, 1 : 1000 solution, one part in 200,000 parts of saline solution. Salt solution, when given alone intravenously under the skin or by rectum, is of little or no benefit in cases of shock, as it does not raise the blood-pressure. All other stimulating drugs, as strychnine, are out of the question for the same reason. In collapse drugs may be employed with advantage, because the vasomotor center needs and can take stimulation to bring it to its proper condition. **Strychnine** may be used. **Alcohol** is of some value, but its stimulating effect is due to the chemical irritation it causes. **Cold**

water on the face, **ammonia fumes**, and **artificial respiration** will do the work. **Salt solution** is indicated if the collapse is due to loss of blood. When shock and collapse are combined, the outlook is unfavorable, but treatment should be along the lines of shock. Caswell (Boston Med. and Surg. Jour., June 28, 1906).

In cases in which shock is not due to hemorrhage, in the earliest stages, the condition can at times be met by the hypodermic administration of **camphor** 1 grain (0.065 Gm.) in oil, **digitalis** 15 minims (1 c.c.), or 15 minims (1 c.c.) of **epinephrin chloride.**

Unless the circulatory failure is distinctly due to cardiac disease and not to vasomotor exhaustion, as is usually the case, strychnine should be avoided, for in shock, as shown by Crile, strychnine rather aggravates than alleviates the condition. Should the skin be leaking badly, the administration of **atropine sulphate** grain 1/100 (0.00065 Gm.) will assist materially.

In some cases all these measures appear to be insufficient and the patient sinks rapidly. At this juncture nothing will tend to revive her as speedily as the slow, continuous intravenous introduction of about 500 c.c. (1 pint) of normal **saline solution** with **epinephrin chloride** 15 minims (1 c.c.), to be followed immediately by the subcutaneous introduction of 1000 to 2000 c.c. (1 to 2 quarts) of salt solution.

In cases of profuse hemorrhage, in addition to lowering the head of the patient, the author employs the same measures, but instead of introducing 500 c.c. (1 pint) of normal saline solution with epinephrin chloride, 1000 or 1500 c.c. (1 or 1½ quarts) are slowly introduced intravenously. One should never try to cut the vein with a knife, but always use a scissors, making a clean cut in a transverse direction.

The most efficient method for combating shock and raising the blood-pressure is the **pneumatic suit of Crile**, but this is rarely at hand. **Bandaging of the limbs** tightly from the extremities upward will in some degree answer the same purpose. **Hot-water bottles** and **hot blankets** should be placed around the patient, and every portion of the body but the operative field should be kept covered and dry. H. S. Wieder (Therap. Gaz., Dec., 1907).

Saline solution must not be pushed if there is hemorrhage which is not yet under control; otherwise more blood may be washed out of the vessels and the condition made worse. If hemorrhage is not a factor **saline infusion** is, on the other hand, an essential measure. The best procedure of all for severe shock, but one not often possible, is **transfusion of blood:** Blood remains in the vessels, whereas saline solution soon leaks out into the tissues.

B. After Anesthesia.—**Vomiting** is a very common after-effect of ether anesthesia. Usually it soon ceases, but in some cases it tends to persist for a number of hours or even days. The incidence of vomiting depends to a considerable extent upon the care with which the patient is prepared for anesthesia and the pains taken to avoid overdosage of ether. In incomplete anesthesia, changing the position of the patient may bring on retching and vomiting.

Accompanying disease is a frequent cause of vomiting. In such cases, if practicable, the operation should be deferred until a suitable time. In persons of a nervous temperament more vomiting ensues upon anesthesia. It is of the utmost importance to have the patient in as peaceful a frame of mind as possible. The room should be absolutely quiet.

In winter time it is best to warm the anesthetic. To do this the author uses a half-glass of hot water and places the bottle into that. The water is changed when necessary. By this method much less anesthetic is used and complete anesthesia is obtained much more quickly.

Uneven anesthesia should be avoided. There is more vomiting from five minutes of an irregular anesthesia than from one hour of an even one. Excessive stimulation by hypodermic injections during anesthesia may be a contributing cause of vomiting.

To diminish the salivary secretion the author rolls up two small hand-sponges and places one in each buccal cavity opposite the second molar tooth (the exit of Stenson's duct). In this manner all the secretions of the parotid gland are stopped. To prevent the patient from swallowing the sponges or the anesthetist from forgetting to remove them, a string may be attached to each sponge and allowed to hang down from the corners of the mouth.

It should be remembered that all body movements increase vomiting—especially so *after* anesthesia. The best method to control postanesthetic vomiting is to keep the patient without moving, in a quiet room, and to administer very small quantities of **hot water**, or very small pieces of **cracked ice**, at frequent intervals. J. Halperin (N. Y. Med. Jour., July 22, 1911).

Vomiting is due to either irritation of the gastric mucous membrane or it may be due to brain conditions or renal conditions. When it arises from cerebral or cerebellar conditions it may be due to the head having been kept at too low a level. Unless there is obvious ischemia of the brain, prolonged depression of the head, especially in plethoric persons, will tend to produce postanesthetic sickness. As soon as the patient has come through the operation, if he is not greatly collapsed he should be kept fairly raised.

Vomiting from the stomach may be due to imperfect preparation of the patient. If the patient is not starved to excess, has no purge for two days before the operation, and has the bowels properly regulated, such vomiting is avoided. In the case of a person who is known to be inclined to vomit, the best plan is to feed by the rectum for twenty-four hours before the anesthetic and to allow copious libations of hot water for three days before.

Renal vomiting is a very serious condition. It is due in general to the operation, though it may be also due to too much anesthetic. Buxton (Clinical Jour., April 24, 1912).

The liability to vomiting is increased when acetone is found in the urine. Protracted vomiting is best treated by **sodium bicarbonate** by bowel and by lavage. These patients need careful watching on account of the liability to acid intoxication. Acetonuria is due to faulty metabolism, and increased by carbohydrate starvation. It has no relation to the length of anesthesia. The duration of anesthesia has only a slight influence on vomiting. Chalfant (Jour. Amer. Med. Assoc., Sept. 14, 1912).

The author does not believe that the presence of ether in the stomach is the cause of postanesthetic nausea. Even if it does, olive oil, as often recommended, can do but little good, for it finally becomes saponified and is absorbed as any other digested fat, possibly carrying into the system again with itself some of the ether to be re-excreted, and liberating a part to play again the rôle of irritant. A better agent is **liquid petrolatum,** which is inert, cannot be saponified and absorbed, and is an excellent protective to mucous membrane. Ferguson (N. Y. Med. Jour., June 29, 1912).

Treatment.—Vomiting during anesthesia can often be controlled by prompt **pressure** with the thumb or finger **on** one of the **phrenic nerves,** viz., posteriorly above the clavicle between the two heads of the sternocleidomastoid muscle, the head being meanwhile turned to the opposite side (Joos).

Vomiting after conclusion of anesthesia may be treated by frequent **rinsing of the mouth with ice-cold water,** by giving the patient small pieces of ice to suck, or by administering teaspoonful doses of very **hot water. Inhalations of vinegar** have also been advised, but are less efficient than the preceding.

> The most satisfactory method of controlling nausea and vomiting after anesthesia is the administration of strong **vinegar by inhalation.** A towel or cloth, saturated with fresh, strong vinegar, is held a few inches above the patient's face, or hung from the bedstead, so that it will be near his head. Rugh (Dunglison's College and Clin. Record, April, 1898).

> Bile being alkaline in reaction, when from relaxation or reversed peristalsis it enters the stomach, though this organ be at rest and therefore covered with mucus, causes an outflow of gastric juice. The acids are set free, with a resultant fluid vomit easily capable of burning the skin. Burns may occur on the mouth and cheek after vomiting of strongly acrid bile-stained fluid. The anesthetist should have at hand a towel saturated with **weak soda solution** to wipe any part touched by vomited matter. Griffith (Med. Record, April 19, 1902).

Gastric lavage is a valuable measure in severe vomiting. Some, in fact, advise its routine use before the patient regains consciousness. It is performed by passing a rubber stomach-tube through the nose or mouth and running in one or two quarts of normal saline solution, the patient's head being meanwhile lowered to prevent returning fluid from entering the trachea.

> Ether is excreted largely by the gastric mucosa, and as long as this is kept up vomiting may occur. By prolonged lavage the ether is washed out of the blood and vomiting is prevented. The tube is kept in the stomach and that organ thoroughly washed out before the patient recovers from the anesthesia. Two and a half or three gallons of water are introduced into the stomach and siphoned out, a pint or a quart at a time. If the patient has nausea after ether he is required to drink a glass of water. Brown (Surg., Gynec., and Obstet., Aug., 1905).

> To prevent fecal vomiting during anesthesia, **lavage** may be employed, and the stomach and esophagus cleaned out with **boric acid solution** and hot water. The next step is to perform **laryngotomy** under local analgesia, or even under light anesthesia. As soon as the larynx is opened, and a **cocaine spray** used to lessen spasm, **chloroform** is to be administered through the laryngeal tube to full anesthesia. The mouth is opened by a gag and a full-sized **esophageal tube** introduced into the stomach. After packing very carefully both the upper opening of the larynx and the pharynx around the esophageal tube, the free end of the esophageal tube must be allowed to drain into a vessel containing a deodorant and antiseptic. It is essential that the tube be introduced and maintained in the stomach, and that the packing round it be tight. Buxton (Brit. Med. Jour., April 23, 1910).

A simpler method of washing the stomach is merely to have the patient drink a glass of **hot water,** which will wash out irritants from the stomach when the patient vomits.

Other measures recommended to allay vomiting are the placing of a **hot-water bag, ice-bag** or **mustard plaster** over the stomach, the repeated administration of 1/12 to 1/8 grain (0.005 to 0.008 Gm.) of **cocaine hydrochloride** in a teaspoonful of hot water, the giving of **sodium bicarbonate,** 15 or 20 grains (1 to 1.3 Gm.) in a glass of warm water, the use of gastric sedatives such as **bis-**

muth subnitrate and **cerium oxalate,** and, finally, general depressant drugs such as **acetanilide, bromides,** and **morphine.** Buxton has recommended the administration of a mixture of 4 or 5 drops of **chloroform** with 2 or 3 drops of **vinegar of opium.**

If, as a cause of vomiting, there has been swallowing of blood or mucus, or there is complaint of the taste of ether, it is best to give a half-pint of **hot water** containing a teaspoonful of **sodium bicarbonate.** This will probably either wash out the stomach into the bowel or cause an effectual and final vomit. It may, however, be necessary to repeat it after an interval. **Black coffee,** to which some add **sodium bicarbonate,** also **iced champagne** in small quantities, have seemed to do good. The taste and smell of ether may be overcome by the use of thin slices of **lemon** and of toilet **vinegar.** For neurotic patients a **mustard leaf on the epigastrium** may be recommended with confidence. When vomiting threatens to be severe or continuous, a detailed examination of the urine should be made, especially after interference with any part of the urinary tract and when acid intoxication may be suspected. If there is atonic distention, **strychnine, pituitary extract,** or **ergotine** (hypodermically) is often effective, and the bowels should be well cleared out by **enemata,** if not acting. A rectal tube may be left in for an hour or so at a time and the **abdomen massaged** if there is no contraindication. Mortimer (Lancet, June 17, 1911).

The administration of 15 grains (1 Gm.) of **chloretone** as a preliminary to anesthesia has been recommended to prevent post-operative vomiting as well as excitement during the induction.

To prevent nausea and vomiting after anesthesia, **chloretone,** in amounts from 5 to 36 grains (0.3 to 2.3 Gm.), given in a 5-grain (0.3 Gm.) capsule, was used in 164 cases. The best results were obtained in adults with 10-grain (0.6 Gm.) doses given twenty to thirty minutes before starting the anesthetic. If it is given inside of twenty minutes the patient is liable to vomit soon after the anesthetic is started, thereby losing all benefit of the drug. While chloretone has not always proved a reliable specific in preventing nausea and vomiting, it has been a great aid. Vomiting, when present, usually took place before the return to consciousness. Beebe (Boston Med. and Surg. Jour., Oct. 6, 1904).

Before beginning the administra- of the anesthetic the patient is given by the author 5 to 6 drops of a 5 per cent. solution of **alypin,** and this dose is repeated as soon as the patient is sufficiently recovered to swallow. This usually prevents all nausea, but if there is a tendency to it the dose may be again repeated in one or two hours. Wanietscheck (Prager med. Woch., Nu. 50, 1906).

To prevent vomiting, the author aims to oxidize the ether as soon as the anesthetic effects are no longer needed by the surgeon. This he accomplishes by administering **oxygen inhalations** immediately on suspension of the anesthetic, and continuing it until consciousness is regained, and in some cases even longer. He has used this method for two years in a variety of operations and always with success. W. T. Wootton (Jour. Amer. Med. Assoc., April 27, 1907).

Endorsement of McArthur's plan, which consists of giving 2 ounces (60 c.c.) of fresh **cold water to drink** after midnight on the morning of operation, repeating this every fourth hour until two hours before operation, when 10 ounces (300 c.c.) are given and repeated just before anesthetization begins. Gunn (Montreal Med. Jour., June, 1907).

Especially in the case of operations done during the first whiffs of ether, the **Bier constricting band, applied to the neck** immediately after the close of the operation and left in place for a half to one hour, while the patient reclines, eliminates vomiting. Ritter (Zentralbl. f. Chir., July 11, 1908).

The most rational way to treat and prevent nausea and vomiting after anesthesia is to promote elimination of the anesthetic. The patient should be kept **warm** so that the skin may act freely, and renal secretion should be helped by **saline enemata,** introduced slowly as soon as the patient is back in bed. While elimination is thus going on, the less put into the stomach the better. Thirst gives little trouble if enemata or subcutaneous injections are used. **Washing out** the **mouth with lemon-juice and water** is pleasant for the patient, and helps to allay thirst. J. Blumfeld (Med. Press and Circular, June 16, 1909).

The author urges that the patient drink an **abundance of water** for two days preceding the operation, and gives **saline enemas** every few hours after the operation to lessen the thirst, nausea, and shock. When not contraindicated by the operation, it is sometimes advisable, when ether mucus has been swallowed, to allow the patient to drink all the water desired as soon as consciousness returns; if this is vomited the stomach is washed out, and if it is retained the ether mucus is diluted. Another method, advocated by Kelly, is to **wash out** the **stomach** thoroughly after the operation, and then leave in it 6 ounces (180 c.c.) of a saturated solution of **magnesium sulphate.** L. F. Watson (Old Dominion Jour. of Med. and Surg., Sept., 1909).

Thirty patients were given **olive oil** by mouth immediately after partial restoration of consciousness following an ether anesthesia. The results were striking. In certain of the cases nausea failed to occur at any time. In a second group in which nausea had begun prior to the administration of the oil it was immediately checked by it. In only 1 patient was nausea observed after giving the oil. E. A. Graham (Jour. Amer. Med. Assoc., Dec. 18, 1909).

The author administers 15 grains (1 Gm.) of **chloretone** in a capsule, one and a half hours before operating. It lessens the patient's dread; the anesthetic is taken more quietly and less is required; the patient comes out quietly (healing by first intention is thus facilitated, ligatures are less likely to slip, and bandages remain undisturbed), shock is markedly reduced, and nourishment can be taken freely as soon as the patient becomes fully conscious. The only drawback is that the drug may cause dizziness before the operation. L. W. Bickle (Therap. Gaz., Mar., 1912).

Respiratory Complications, especially frequent after ether, occur in the form of bronchitis, lobular or lobar pneumonia, and edema of the lungs. They have been ascribed to irritation by the anesthetic, undue exposure of the patient to cold, and the inhalation of vomitus or septic fluids during the operation. Doubtless in many instances several of these causes have been simultaneously operative.

Acute edema of the lungs is one of the immediate sequels of ether narcosis, and, while comparatively rare, it must be reckoned with. In the case reported by the author the whole process appeared to have originated in the air-vesicles, and to have run its course and ended there. The most effective features in the treatment during the crisis were a large dose of **nitroglycerin,** moderate elevation of the foot of the bed, and very active **dry-cupping** all **over** the **chest.** The patient recovered. Any exposure during operation which tends to check active perspiration is very dangerous to both the lungs and kidneys. Pedersen (Annals of Surg., Jan., 1906).

Study of 2500 cases of ether anesthesia, in nearly all cases with the Clover inhaler: 55, or 2.2 per cent., developed some lung complication;

32, or 1.28 per cent., came to autopsy; 35 occurred during the cold months of the year. The lung complications all developed within forty-eight hours; 37 cases had some septic focus before the development of the lung complications. In 8 cases the presence of emphysema was noted, in 1 there was chronic bronchial asthma, and in 9 cases chronic nephritis was present. There were 14 cases of lobar pneumonia, 16 of bronchopneumonia, 19 of bronchitis, 3 of plastic pleurisy, 1 of pleural effusion, and 2 of empyema.

On the whole, the administration of ether *per se* was not a very active cause. In nearly all instances other more highly probable etiological factors were present, such as aspiration from the mouth and pharynx, and the operation performed, abdominal operations predisposing markedly to these complications. Armstrong (Brit. Med. Jour., May 19, 1906).

Lobar pneumonia following anesthesia differs from that commonly seen in lower and more irregular temperature, shorter and rarely a true crisis, greater freedom from complications, central type, lung signs developing late and cough not marked or severe, and sputum rarely blood tinged. In most cases more than one theory is necessary to explain the origin: 1. Irritant action of anesthetic; ether is the most irritant, chloroform the least. 2. Aspiration of mucus and vomitus and hypersecretion of mucus. 3. Emboli. 4. Toxic effect on heart and blood-vessels; chloroform is the most dangerous. 5. Presence of pneumococci and other bacteria in mouth and throat. 6. Extension of infection through subdiaphragmatic space. 7. Cooling of the body; a loss of temperature from a half to one degree may follow prolonged anesthesia without any other factor. 8. Limitation of lung expansion. 9. Lessened resistance of the patient. Prevention lies in disinfection of the mouth and nose as a routine measure, and administration of the anesthetic by the open drop method with the head low and to one side, and the jaw kept forward. The patients must be kept warm and dry by warm pads, jackets, and leg covers. Wight (Bull. Johns Hopkins Hosp., March, 1908).

Complications on the part of the lungs follow in about 5 per cent. of all laparotomies. The essential factor is the impossibility of adequate expectoration after the operation. Chilling probably also contributes, and the author has devised a contrivance to add to the apparatus for mixed oxygen and ether or chloroform inhalation anesthesia, which warms the fumes. A. Läwen (Münch. med. Woch., Oct. 3, 1911).

Such complications are particularly likely to occur, however, where predisposing conditions such as bronchitis, emphysema, old age, and general enfeeblement already exist.

Ether occasionally causes a latent tuberculous process to break out afresh.

The *treatment* of the respiratory complications is that classically recommended for the conditions present. The reader is referred to the articles on PNEUMONIA, BRONCHITIS, etc., for information in this direction.

Renal Complications.—Irritation of the kidneys, as shown by the appearance of albumin, casts and occasionally red blood-cells in the urine, may be observed after ether as well as after chloroform.

In 65 chloroform cases the urine showed albumin or casts (or both) induced or increased after inhalation in 40 per cent. of the cases, sugar occurring in 1 instance. In 61 cases of anesthesia produced by nitrous oxide followed by ether, albumin and casts occurred or were increased in the urine in 12 per cent., 1 case showing sugar. In 41 cases of chloroform followed by ether, albumin and casts were induced or increased in 41.5 per cent. of the cases. In 28 ether anesthesias, 39 per cent. of the cases showed albumin and casts increased or present afresh after the narcosis, 2 cases also showing fresh occurrence of sugar in small quantities. Goodwin (Therap. Gaz., May, 1905).

Where renal disease already existed beforehand, suppression of urine may occur, and the condition of the kidneys be made worse.

The early effect of both ether and chloroform up to the period of complete insensibility is ordinarily an increase of the secretion of urine. This, as a rule, is more pronounced in the case of ether than of chloroform, but during full anesthesia, however prolonged, the secretion of urine is almost completely arrested. The depressing effect during this period is more pronounced with ether than with chloroform. On removal of the anesthetic the kidneys rapidly recover, and there is hyperacidity lasting for some hours. Thompson (Brit. Med. Jour., March 25, 1905).

During ether narcosis the volume of urine secreted is affected in two ways. In most instances there is a decrease, in a few an increase. The latter is probably an early or light effect, the former a pronounced effect. The maximum outflow of urine occurs about three hours after discontinuance of the anesthetic. With ether the urine when diminished in volume is, as a rule, more concentrated (contains more nitrogen). The converse is the case with chloroform. Arrest of urinary secretion occurs more readily and with a relatively higher blood-pressure in ether than in chloroform narcosis. The escape of leucocytes into the urine after full ether narcosis is more marked than with chloroform, probably indicating a higher degree of stasis in the glomerular capillaries. An increased excretion of chlorides is seen after ether inhalation, but much less and of shorter duration than in the case of chloroform. Thompson (Brit. Med. Jour., March 24, 1906).

The effect of chloroform and ether on the kidneys is merely one manifestation of a general intoxication of the system from the drug. The old theory of a delayed toxic action on the kidneys has been sustained by recent research, which has revealed degeneration of the parenchymatous organs throughout, but most prominent in the kidneys. The least harmful of all techniques is general anesthesia with ether plus **oxygen,** preceded by an injection of **morphine.** Under all conditions the amount of the anesthetic used should be the smallest possible. Loss of blood should be combated in every possible way. The interval between successive anesthesias should be at least a week, and the second anesthesia should never be attempted until the urine is free from albumin and has lost its transient reducing power. M. Hirsch (Centralbl. f. d. Grenz. d. Med. u. Chir., Dec. 31, 1908).

The *treatment* of renal complications after ether comprises **saline enteroclysis,** the administration of **purgatives** and unirritating **diuretics,** and other measures commonly employed in similar states otherwise arising.

Late Poisoning.—Disturbances of metabolism, due to persisting effects of the anesthetic upon the cells of parenchymatous organs, especially the liver, kidneys and heart, and culminating in acid intoxication, with marked restlessness, vomiting, delirium, convulsions and coma, sometimes followed by death, occur much more rarely after ether than after chloroform. The symptoms typically begin only a number of hours or two or three days after the anesthesia, and in fatal cases progress rapidly to a termination. This condition, with its treatment, has been fully discussed in the article on CHLOROFORM (Vol. III), to which the reader is referred.

In the fatal cases of late intoxication, death is almost invariably due to chloroform; ether is seldom the cause of a death of this kind. Bevan and Favill (Jour. Amer. Med. Assoc., Sept. 2, 1905).

Operations should be delayed when possible if a fatty liver be suspected, *e.g.*, in subjects of rickets and infantile paralysis who have been overfed with fattening food and underexercised; in cases of sepsis and diabetes, and when a history of cyclic vomiting is obtained. When a child has recently vomited apparently without cause, an intended operation should be postponed. When fatty liver is suspected the patient should be kept for some days on a diet restricted in fat. **Bicarbonate** or **citrate of soda** should be given. Mild purgation may be beneficial. Starvation will cause acute acetonuria; therefore nutrient enemata should be given two hours before and immediately after an operation. The treatment of acid intoxication following operations should be by **venesection, saline transfusion,** and **clysters of solution of bicarbonate** of **sodium.** L. G. Guthrie (Clinical Journal, June 12, 1907).

The old treatment of postanesthetic acidosis was to give alkalies, but that line of action no longer appears convincing. The disease is due to exhaustion of the liver and to damaged tissue, and the treatment is to give **glucose,** if possible by the mouth, or, failing this, by rectal injection; treated in this way, these cases do, as a rule, extremely well. Buxton (Clin. Jour., April 24, 1912).

Postanesthetic Paralysis.—This is a complication only indirectly due to the anesthesia, and consisting in loss of function of certain nerves due to pressure upon them by reason of faulty positions of the patient during operation or to the resting of limbs on the edge of the table. The most common paralysis occurs in the arm, and is due to pressure exerted upon the musculospiral nerve as the arm hung down beyond the table-margin. The brachial plexus may also be affected, owing to pressure from the head of the humerus in a case where the upper extremities have been kept above the head during the operation.

Postoperative paralysis results from temporary pressure of the head of the humerus on the infraclavicular portion of the plexus, due to hyperelevation of the arm, with rotation inward. The author favors Holst's method of securing the arms at the sides, resting on cushions. Glitsch (Zentralbl. f. Gynäk., Nu. 39, 1904).

Paralysis of nerves of the leg or face also occasionally occurs. The paralysis is not generally permanent. In rare instances, more widespread paralysis follows operation, owing to cerebral hemorrhage or embolism resulting from the primary stimulating effect of ether on the circulation.

Anesthesia paralysis occurs in two forms, peripheral and central. The peripheral may be averted by proper treatment during narcosis. The central cannot be prevented, though its danger may be avoided by limiting the quantity of anesthetic and by a preliminary hypodermic of **morphine** in ether anesthesia or ether narcosis, to control excitement. Halstead (Wisc. Med. Jour., Feb., 1908).

ANESTHESIA BY INTUBATION AND INTRATRACHEAL INSUFFLATION.—In cases where anesthesia with the mask is difficult and where it is earnestly desired to use as little of the anesthetic as possible, Kuhn introduced a method consisting in intubation of the larynx and connection of the intubation tube with a rubber tube attached to a funnel covered with gauze, on which the anesthetic is dropped. By this procedure there is gained absolute control of the amount of anesthetic administered, and relief from the risk of swallowing blood as well as from the necessity of frequently interrupting anesthesia in facial, nasal, and buccal operations.

Good results obtained with Kuhn's method of intubation anesthesia in 7 extensive operations on the head. The patients were all chloroformed in the usual manner, and a mild degree of asphyxia was produced. The tube was then introduced in the manner prescribed by Kuhn, the mouth being opened by Heister's or O'Dwyer's instruments and the tongue held forward by forceps. One recognizes if the tube is in the larynx by the stridulous breathing, which immediately ceases when the mandarin is withdrawn. The fastener or joint for the rubber tube must then be turned toward the side opposite to that on which the operation is to take place, so that the metal spiral tube may be brought out of the mouth at the angle. Then after the tube is fixed, the funnel is applied and, lastly, the packing of gauze is placed around the tube in the larynx. The anesthetist can control the respiration well by auscultating through the funnel and tube. **Chloroform** was given at first, and continued after the intubation until the anesthesia was satisfactory, and then ether was substituted, care being taken to use the proper dose. The method is of special advantage because the operator and anesthetist are entirely independent; the latter is able to keep up an equable anesthesia with a minimum quantity of anesthetic and no blood can get into the larynx. No bad effects from the intubation were seen after the operations. A. Dirk (Deut. med. Woch., Oct. 4, 1906).

Technique of tubation of pharynx to facilitate administration of anesthetics described: The patient is reduced to complete surgical anesthesia in the usual way. The pharynx is then cleansed by a small gauze sponge held by a long pair of forceps and cocainized with a 0.1 per cent. solution of **cocaine.** Two rubber tubes as long as will pass, thereby fitting snugly, cut on the bias and fenestrated laterally near the ends, are inserted into and through the nares as far back as the epiglottis, which will be felt as an obstruction to further passage of the tubes. The mouth is then widely opened and the tongue drawn well forward and out. With one good-sized sponge the entire pharynx is then packed, while making traction upon the tongue, as far back as the tubes. This forms, when in position and properly packed, an air-chamber or space in which the tubes and larynx communicate. The tubes are severed an equal distance from the nose. The anesthetist listens carefully to ascertain if the patient is breathing through the tubes. If not, the gauze packing in the tubes is too deep, allowing no space for air, and should, therefore, be repacked until rhythmical breathing is heard through the tubes. The tubes are now joined by a Y-shaped hard-rubber tube to which is attached by means of another rubber tubing a hard-rubber funnel covered with two to four thicknesses of gauze. The anesthetic is then administered by pouring upon the gauze funnel. Aspiration of blood and vomitus is impossible, and the mucus forming in the throat is absorbed by the gauze sponge, which further acts as a hemostatic because of its pressure upon the base of the tongue, controlling to a great extent the hemorrhage, excepting in operations in which the lingual arteries have been severed. The head may be placed in almost any position advantageous to the operative technique regardless of resultant hemorrhage. The author emphasizes the necessity of using considerable gauze in packing the pharynx, so much as almost to fill the space; then subsequent loose packing of the remainder. McHenry (L. I. Med. Jour., Feb., 1907).

Description of an apparatus used in nearly 1000 tonsil and adenoid operations and providing for continuous etherization without in any way interfering with the operation. It consists of a vaporizer which is worked by a foot-pump and of several accessory implements which may be connected with the vaporizer by a long rubber tube. The apparatus will vaporize 15 ounces of ether in an hour and will readily provide sufficient anesthesia in an adult with the face uncovered for a laparotomy of an hour's duration. Miller (Boston Med. and Surg. Jour., July 15, 1909).

In 1909 Meltzer and Auer discovered a new method of effecting artificial respiration which later on proved in addition highly advantageous, under certain circumstances, for the administration of anesthetics. The principal feature is that, by means of a tube passed into and fitting loosely the trachea, ether-laden air is led in a nearly constant stream approximately to the tracheal bifurcation. So perfect an artificial ventilation of the lungs is thus secured that the respiratory movements become largely or wholly unnecessary, and correspondingly cease. Either or both sides of the thorax can now be entered for surgical procedures without any ill-effects from the resulting pneumothorax. The diminished number of respiratory movements, furthermore, facilitates the performance of such procedures. A very complete aëration of the intrapulmonary surfaces is insured by this method, and the patients therefore recover quickly from the anesthetic.

The apparatus required, in its simplest form, consists merely of a foot-bellows, a Wolff bottle, a mercury manometer, and a soft-rubber catheter. These are united by rubber tubing so that air can be forced through ether in the Wolff bottle and thence through the catheter into the lungs, while the pressure of the air-current is constantly indicated by the mercury manometer.

The apparatus described consists of a Wolff bottle with three necks placed within a copper water-jacket, and a foot-bellows. By means of cocks the stream of air can be carried through the hot water, over the top of the ether in the Wolff bottle, or through the ether when a particularly strong vapor is desired. Air and ether vapor may be mixed in any proportion. Connected with the delivery end of the apparatus is a safety valve and pressure regulator consisting of a bottle of mercury into which a tube is plunged. The depth of the tube in the mercury, which is adjustable, represents the maximum of pressure which is allowed within the apparatus; if for any reason the pressure should rise, the valve "blows off" automatically.

The air or mixture is supplied at a practically constant temperature of about 10 degrees above room temperature. As an intratracheal tube the author uses a French lisle catheter, 22 to 24 F., moistened in hot water to render it pliable, a new and sterile one being used for each case. For the introduction of the tube, he uses a laryngeal forceps with sleeves attached for grasping the tube near its extremity. Ehrenfried (Boston Med. and Surg. Jour., April 13, 1911).

The technique of the insufflation anesthesia is as follows: The patient having first been anesthetized in the ordinary way, a 10 per cent. cocaine solution is sprayed over the pharynx. With the head extended over the end of the table, and the tongue pulled forward, the glottis is held open with the forefinger of the left hand, while the right passes into the trachea a catheter having a diameter about one-third that of the canal. Too large a catheter causes shallow breathing and cyanosis under small pressure, whereas one too small fails to keep the patient under. For the average adult a catheter No. 22 to 28 French is suitable. It is passed down to within one inch of the bifurcation, which measures on the catheter about 26 cm. from its tip.

Description of an introducer for the racheal tube, following nearly in curve and angle the O'Dwyer apparatus. When the patient is etherized fully with inhaler or cone, a mouth-gag is inserted on the patient's left, the tongue dragged forward sharply with tongue forceps, the operator's left index finger thrust down until it meets the epiglottis, and the introducer, held in the right hand, is pushed in and down, alongside the left forefinger, till it has passed the upper projecting edge of the epiglottis. Then the heel of the instrument is pitched upward, and the assistant feeds the catheter into the larynx and trachea. At first nitrous oxide was given with the usual oxygen coefficient till consciousness was lost, and anesthesia then deepened by the addition of ether till the laryngeal reflex was abolished, when the intratracheal tube was introduced. Cotton and Boothby (Surg., Gynec., and Obstet., vol. xiii, p. 572, 1911).

Two methods of introduction of the tube have been in use—that of direct inspection through a Chevalier-Jackson laryngoscope; and by means of a specially constructed introducer in which the tube is threaded through a tunnelled urethral sound with an O'Dwyer curve to hook over the arch of the tongue. The tube should be 22 F. for most adults, occasionally 24 in thoracic cases, to insure a return flow of air not too great for the maintenance of sufficient intrapulmonary pressure. If the tube is so small as not to provide for sufficient pressure to keep the lung inflated when the chest is open, according to Meltzer pressure just below the thyroid notch, at the middle of the thyroid cartilage, every few minutes will remedy the defect. Woolsey (N. Y. State Jour. of Med., April, 1912).

The bellows are then attached and a mixture of air and ether pumped in a steady stream into the trachea under a pressure of about 12 mm. of mercury. The catheter, by partially obstructing the outflow of air and ether, raises the intrathoracic pressure. When the thorax is open the lungs may be collapsed or distended at will by decreasing or increasing the pressure. The respiration becomes shallower as the pressure is raised (H. H. Kerr).

Elsberg has devised and uses an electrically driven, improved form of the apparatus above referred to, while H. H. Janeway still more recently has described a further improvement and elaboration (Fig. 7) of the original mechanism, which is so planned as to supply a current of warmed, moistened and filtered air, containing any desired amount of ether vapor, and interrupted at regular intervals. The interruptions in the flow are very important in that they not only assist the diffusion of oxygen in the lungs, but overcome the tendency to obstruction of the venous return flow to the heart resulting from the pressure of the constantly distended lung on the great veins. Janeway's apparatus is also provided with a blow-off safety-valve, to guard against injury to the papatient's lung if an accidental marked rise of pressure should take place owing to faulty introduction of the tracheal tube. Foot-bellows are always to be kept at hand for use in case the electric current actuating the motor should happen to give out.

From the moment the power is turned on and the pressure regulated,

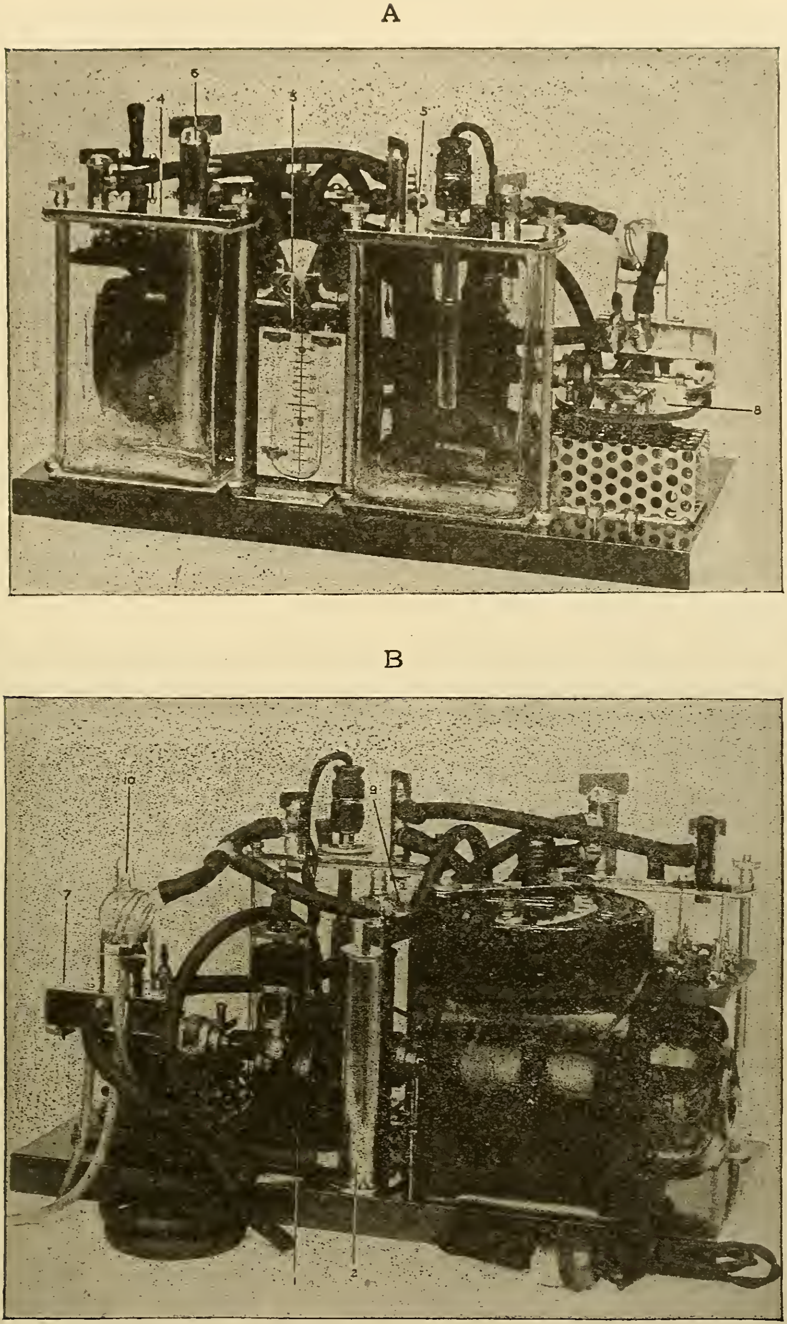

Fig. 7.—Janeway's apparatus for intratracheal insufflation. *A*, front view. *3*, valve for regulating the amount of air passed over the surface of the ether; *4*, ether jar; *5*, water jar; *6*, valve for bubbling a portion of the air through the top layers of the ether: *8*, worm wheel operating interrupting valve. *B*, back view. *1*, blower: *2*, air filter and muffler; *7*, interrupting valve; *9*, safety-valve controlling the pressure; *10*, condensing bulb.

(Annals of Surgery.)

the anesthetist has nothing to do but watch the pressure gauge and occasionally interrupt the current of air so as momentarily to collapse the lungs. The tracheal tube must be fairly rigid so that it cannot be coughed out when once in place. This requirement is best met by a silk-woven catheter. It should have an opening at or near its end and must be at least 30 cm. long. The ordinary silkworm urethral catheter will do very well, and has the advantage that it can be obtained anywhere. The catheter should have two marks upon it, one 12 cm. from the tip, and a second 26 cm. from the tip. Therefore, if the tip of the intratracheal tube is 26 cm. from the incisior teeth, it will lie 5 cm. or less above the bifurcation of the trachea. For the adult it is advisable to use a tube whose diameter measures about one-half of the length of the glottis as seen through a direct laryngoscope. The author insufflates pure air for a few minutes at the end of the anesthesia so as to blow out the anesthetic from the lungs and trachea. So quickly will the patient react that one must be careful that he is receiving enough ether mixed with the air during the operation. C. A. Elsberg (Annals of Surg., Feb., 1911).

From observations in 216 cases the author regards insufflation anesthesia as safe if certain cardinal principles are observed in its administration, viz., one must guard against overpressure, spraying of liquid ether through the tube, introduction of the tube into the esophagus, introduction of the tube beyond the bifurcation of the trachea, and trauma to the pharynx or larynx in intubation. Proper apparatus and ordinary caution should absolutely prevent the accidents responsible for the few deaths reported from the method. The uniformly sufficient aëration of the lungs, with the even administration of well-diluted ether vapor, relieves the respiratory apparatus and central nervous system of much strain, and overetherization is impossible. Peck (Annals of Surg., July, 1912).

Endotracheal insufflation anesthesia, properly administered and safeguarded, can be rendered devoid of intrinsic danger. It is indicated whenever the operation is about to interfere in any way with the ability of the patient voluntarily to respire. Of the various anesthetics to be used with this method, ether with air is the most applicable for general use; however, **nitrous oxide oxygen** with minimal quantities of ether may occasionally be the anesthetic of choice. To prevent deaths from emphysema, the apparatus must be provided with a safety-valve by which the endothoracic pressure cannot exceed 15 mm. Hg. Cotton and Boothby (Annals of Surg., Jan., 1913).

Woolsey enumerates the indications for intratracheal anesthesia as follows: (1) Intrathoracic surgical cases where its positive intrapulmonary pressure presents acute pneumothorax. (2) That class of cases where the obstruction to breathing exists in the air-ways between the teeth and the trachea, from collapsed alæ nasi, recedent jaw and tongue, or paralyzed soft palate and glottis, and in which narcosis is generally maintained in spite of serious anoxemia. (3) In cases where the factor of safety is lowered by age or disease. (4) In all operations of serious nature about the oral or nasal cavities, where aspiration of blood and tumor material would be a source of danger.

Report of a case in which operation was undertaken for a **large sarcoma beneath the clavicle.** Under ether narcosis a catheter was easily introduced into the glottis. Laughing gas and ether anesthesia was continued through the catheter. The operation lasted about an hour and only 100 gr.

of ether were required. The patient's condition remained good throughout the operation and a necessary incision of the pleura was borne without the slightest disturbance. E. Unger (Berl. klin. Woch., Sept. 19, 1910).

Intratracheal insufflation anesthesia found very useful in **operations on** the **neck,** such as **thyroidectomy.** The operator can manipulate the trachea as much as necessary without causing disturbance in breathing or interfering with the anesthesia. Nor need he fear a sudden collapse of the trachea during the removal of a large **goiter.** The method is of great value in operations on the tongue and mouth and in operations on the superior and inferior maxilla, in which the buccal cavity or pharynx has to be widely opened. There is no danger of aspiration of blood into the lungs, and tamponade of the larynx is unnecessary. The current of air continually flowing upward in the trachea by the side of the tube will blow out all blood tending to run down into the larynx and trachea. The anesthesia should be advantageous in **operations on the brain** and the **spinal cord,** such as bilateral suboccipital **craniotomy** and **laminectomy,** in which the patient has to be in the prone position. Elsberg (Annals of Surg., June, 1911).

Tracheal insufflation anesthesia offers the best available conditions for progress in surgery of the **thoracic cavity.** Nitrous oxide and oxygen can be successfully exhibited through the intratracheal tube. Unfavorable results that have been reported have had their origin in easily remedied faults of technique. Use no force in the introduction of the tracheal tube. Use only the lowest concentration of ether compatible with narcosis. Never insufflate without an efficient and suitable mercury manometer and safety-valve that will register a maximum of 20 mm. of mercury. W. C. Woolsey (N. Y. State Jour. of Med., April, 1912).

Report of 2 cases in which Meltzer's method of intratracheal insufflation was applied, proving in one a direct life-saving measure. This was an operation for **sarcoma** of the **nasopharynx, orbit,** and **maxillary sinus** which had twice recurred after removal. The first symptoms had been noted eight months before. With the intratracheal Meltzer technique the operation was conducted safely and more radically than had previously been possible. R. Alessandri (Policlinico, Sept. 8, 1912).

Intratracheal insufflation anesthesia used in almost 500 cases of all kinds. Outside of its special field, **thoracic surgery,** the author has found it of great value in cases of **intestinal obstruction,** for it completely does away with the dangers of aspiration of vomited matter. It seems particularly well borne by very weak and cachectic patients. In **goiter** operations it prevents cough and tracheal collapse. In those patients with a **chronic bronchitis** or some pulmonary trouble, it seems entirely to do away with the danger of subsequent pneumonia. Elsberg (N. Y. State Jour. of Med., Sept., 1912).

Some of the advantages of the intratracheal procedure in ordinary anesthesia are as follows: Prolonged anesthesia appears to be harmless; there is no rattling of mucus in the throat; cough and lung complications are not produced, and postoperative vomiting is absent.

In all the positive and negative pressure contrivances hitherto used, expiration takes place at a disadvantage, the barometric pressure which exists on the surface of the exposed lung being less than that within the air-spaces. This throws an increased amount of work on the right heart, which must compensate. Besides this, there is a tendency for carbon dioxide to remain too long in the alveolar spaces, to the exclusion of the better oxygenated air. In the course of a long operation this has a definite poisoning effect on the heart wall. Both these undesirable effects are avoided by the intratracheal insufflation method. Reference made to the great importance of the insufflation method, using plain air or oxygen, for cases of cessation of respiration from any cause. The lives of patients suffering from **brain abscess** and **morphine poisoning** have already been saved by it. For anesthesia, the sterile tracheal tube should be introduced, either by a laryngeal forceps, the epiglottis being held forward by the operator's left forefinger, or by the use of a Killian speculum. Previous painting of the pharynx and larynx with cocaine is unnecessary. After passing the glottis, the tube is pushed forward till a resistance is felt, or until 26 centimeters have been introduced (in male adults), as measured against the upper incisors. It should then be withdrawn about 1 centimeter so as to lie just above the bifurcation, and connected with the rest of the apparatus. When it is correctly placed, air can be heard to enter both lungs on auscultation. Quimby (Boston Med. and Surg. Jour., Oct. 19, 1911).

In all but a few of 200 cases, the anesthesia was very satisfactory, particularly free from complications and after-effects. It is very easy to keep the patients under full anesthesia, vomiting has never occurred during the anesthesia, and the patients were never too deeply under the ether. Postoperative vomiting was rare, and the patients did not complain of pain or discomfort in the laryngeal region. Elsberg (Annals of Surg., Dec., 1911).

Intratracheal insufflation anesthesia employed in 25 cases. The patients recovered more quickly, the after-effects were lessened, vomiting was only noticed once, and from the surgeon's point of view the anesthesia was perfect. The anesthetist has a greater sense of security, for if at any time he thinks that artificial respiration may be necessary, he has the apparatus ready at hand and has merely to turn the pointer from "ether" to "air." R. E. Kelly (Brit. Med. Jour., July 20, 1912).

INTRAVENOUS ANESTHESIA.—In 1909 Burkhardt advanced the view that it is unnecessary for an anesthetic to pass through various tissues before entering the blood, and that the most direct and satisfactory method of anesthesia is to introduce the drug directly in the blood-stream. In his first trials with ether in 33 human cases, a 5 per cent. solution of the drug in normal saline solution was used. No cardiac or respiratory disturbances were observed, and almost no after-effects—such as headache and vomiting—were met with. No abnormality of the urine, and no thrombosis or other bad result, were noted.

In 4 of the 33 cases, however, it was not found possible to secure complete abolition of the reflexes. The amount of fluid injected ranged from 200 to 800 c.c. Recovery from anesthesia was rapid. Morphine and scopolamine were generally injected before beginning the intravenous anesthesia.

> Children require 10 to 17.5 c.c. (2½ to 4½ drams) of 5 per cent. ether for complete anesthesia; women 10 to 30 c.c. (2½ to 7½ drams), and men 10 to 40 c.c. (2½ to 10 drams). As soon as the reflexes begin to return, it is only necessary to open the cannula and allow 30 to 70 c.c. (7½ to 17½ drams) more of the solution to flow into the vein. Narcosis is complete in eight to ten minutes, and the stage of excitement is usually very short. All the disagreeable by-effects of ether anesthesia, such as cyanosis and disturbances of respiration, rattling in the throat, etc., are absent. The author highly recommends intravenous anesthesia in affections of the cardiac and respiratory organs, and in feeble and debilitated individuals. It is also excellent in **operations** about the **head** and **neck**. L. Burkhardt (Münch. med. Woch., Nov. 16, 1909).

Since in inhalation anesthesia the anesthetic is absorbed from the vapor introduced in the air-passages, the dose actually entering the blood is variable, being subject to all the accidents of laryngeal spasm, respiratory spasm, and variations in the depth of respiration. The exposure of the respiratory tract to an irritating vapor is a serious drawback. The absorption of the drug by the patient cannot be stopped abruptly, but must go on until the patient has rid himself of the vapor which fills his lungs and of the anesthetic-sodden mucus in his bronchial tubes and stomach. In operations on the mouth, jaws, or pharynx the labors of the surgeon are made much harder by his having to share the field of operation with the anesthetist. By direct administration of an anesthetic by the blood all these difficulties are disposed of. The author has given ether infusion anesthesia in 136 cases, using a 5 per cent. solution in normal saline and an apparatus provided with an indicator. The introduction of the cannula must be carried out with the strictest aseptic precautions. Induction of anesthesia is usually quite smooth and rapid, three or four minutes on the average. The chief features of the anesthesia are regularity and smoothness, the ease with which it can be graduated, and the great rapidity of response to slight alterations in dose. Of the 136 patients, only 6 vomited, and of these 3 had swallowed blood during the operation. The advantages of the method were most striking in patients in extreme inanition —*e.g.,* those with abdominal malignant disease. These often left the table in much better condition than before. In any case likely to be benefited by a saline infusion, either as a means of relieving shock or hemorrhage, or because shock is expected, the method has given excellent results. Relaxation of the abdominal wall equal to that produced by any other anesthetic, excepting stovaine, could be obtained. In throat and nose operations in which a more or less vertical posture is essential, an even narcosis can be obtained without congestion or danger of syncope. F. Rood (Proceedings Royal Soc. of Med., April, 1912).

Since that time numerous surgeons have taken the method up, using not only ether, but various other drugs, sometimes in conjunction with the ether. The procedure now most generally followed is that of Rood: A 5 per cent. solution of ether in filtered normal saline solution flows from a 2-liter reservoir, adjusted on a stand eight feet above the floor, through an indicator (in which the amount of solution being used at any given time can be observed), then through a warming chamber into a blunt cannula and so into the vein. The indicator consists of a cylindrical or globular glass bulb of a capacity of 2 to 4 ounces with an inside pipette, very much as in Murphy's apparatus for proctoclysis. When the apparatus is working properly, the lower half only of the indicator is filled with solution. The solution flows from the tank through the pipette and drops on the surface of the fluid in the lower half of the indicator. By means of a compression tap below the indicator, the rate of flow is accurately controlled. The patient's arm is bound to a padded splint, the bend of the elbow wiped with a 5 per cent. solution of thymol in carbon tetrachloride, and the skin anesthetized with 1.5 per cent. cocaine, the median basilic exposed through a small incision and a small blunt cannula inserted. The ether solution is at first administered at full flow, then reduced at the appearance of the usual signs of surgical anesthesia—in from one to five minutes. The solution now drips in a very fine stream or at the rate of 40 to 60 drops a minute, the corneal reflex affording a reliable guide for administration. The customary attention should be paid to maintaining an open airway for respiration, and furthermore, as in inhalation anesthesia, economy in the amount of ether solution administered is of paramount importance. The infused fluid must be kept at a temperature not higher than 90° F., otherwise the ether volatilizes and escapes.

> The best temperature for infusing the ether solution intravenously is 38° C. (100.4° F.). Ether is soluble at this temperature only to the extent of 4.68 per cent. With lower temperature more ether will dissolve, and there is always danger of hemoglobinuria with more concentrated solutions. The advantages of intravenous ether narcosis are especially apparent in operations on the face and in cachectic patients. Loss of blood is better tolerated, the pulse remains stronger, and the patients do not complain so much of thirst after the operation. R. Hageman (Münch. med. Woch., July 11, 1911).
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> Experience with intravenous narcosis in 250 cases. The author employed, in connection with ether, a variety of hypnotics, including urethane, hedonal, chloral hydrate, isopral, chloralamide, veronal, and veronal-sodium. He regards ether in combination with **isopral** as the most effective method of intravenous anesthesia. These agents are separately infused. At first a 1.5 per cent. solution of isopral is instilled in amounts of about 40 c.c. (10 drams) to the minute, the total amount introduced ranging from 100 to 200 c.c. (3⅓ to 6⅔ ounces). This is followed by the ether. Intravenous anesthesia is contraindicated in cases of myocardial degeneration, severe arteriosclerosis, nephritis, marked icterus, cholemia, general congestion and plethora. On the other hand, it is particularly indicated in conditions of collapse, profuse loss of blood, cachexia, debility, disturbances of the respiratory organs and peritonitis, as well as in **operations** on the **head** and **neck**, including the buccal and pharyngeal cavities. L. Burkhardt (Münch. med. Woch., Nov. 15, 1911).
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> Intravenous anesthesia is indicated in operations about the head and neck, in hemorrhage, in weak cachectic patients, in diseases of the respiratory tract where inhalation anesthesia is objectionable, etc. It is contraindicated in nephritis, extreme arteriosclerosis, severe heart lesions, plethoric patients, etc. In the author's opinion, its chief field of usefulness will be found in **operations** about the **neck.** Dodge (Boston Med. and Surg. Jour., Dec. 28, 1911).
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> A total of 498 cases of intravenous ether anesthesia are now on record, with 2 deaths, 1 of unknown cause and the other a case of embolism reported by the author, while Küttner has reported a case of clinically diagnosed embolism. The author thinks there can be no doubt that the fatality in his case was the result of the infusion, but whether the ether was responsible for it or the salt-solution vehicle was not absolutely certain. He infused 810 c.c. (27 ounces) of normal salt solution containing 5 per cent. of ether. Löfberg (Hospitalstidende, May 8, 1912).
>
> The intravenous ether method is especially useful in **operations on the head, throat,** and **neck,** as the anesthetist does not encroach on the field of operation. It answers well in cachectic patients generally, and may be employed with advantage in collapsed abdominal cases and in operations attended by surgical shock, such as those for **ruptured ectopic gestation, Wertheim's operation, removal** of the **breast,** etc.—that is, in cases where saline transfusion is beneficial. In a case of the author's in which **ileosigmoidostomy** was performed there was absolutely no vomiting after the operation, although there had been a great deal of necessary manipulation of the intestine.
>
> The procedure is contraindicated in the alcoholic, plethoric, and muscular type of patient, in cases where there

are advanced changes in the vascular and pulmonary systems, and in all cases in which transfusion would increase backward pressure on the right side of the heart.

The advantages over inhalation anesthesia in selected cases are: The patient is spared the disagreeable sensations; there is no primary irritation of the respiratory organs or of the heart; a very small amount of anesthetic is used; anesthesia, when produced, is of a calm and placid nature; there are no after-effects; headache and vomiting practically never occur, and pulmonary complications are absent. F. L. Napier (Glasgow Med. Jour., July, 1912).

Report of 26 cases of ether anesthesia, using Burkhardt's method of a continuous flow into a vein of a 5 per cent. ether solution, alternating with a **normal salt solution.** The anesthesia was prompt and in every way satisfactory, with no untoward effects. Vostifeeva (Roussky Vratch, Sept. 8, 1912).

The author describes an apparatus for **intravenous ether anesthesia** in which the temperature of the solution is easily regulated by means of an electric bulb, all gas-bubbles are isolated from the solution before entering the vein, and all danger of infection is avoided. Cold, sterile, physiological **salt solution** is filtered through sterile filter-paper into a sterilized bottle up to a graduated mark at 2325 c.c. (2⅓ quarts) and 175 c.c. (5⅔ ounces) of ether is then added, making 2500 c.c. (2½ quarts). After being heated in a copper coil, the solution passes through a "gas separator" and reascends to the original container, whence it is drawn off by a short tube into the vein.

The average requirement for an operation lasting one or two hours is 1 to 1½ liters (quarts) of the ether-salt solution, and 2 liters have been given with absolutely no untoward effects.

The patient goes to sleep on 250 to 500 c.c. (½ to 1 pint) in from eight to ten minutes. As soon as complete relaxation is obtained the solution may be kept shut off over half the time. When the patient shows signs of restlessness, about 25 c.c. (6 drams) of solution gives a very prompt response. This advantage over the inhalation method is due to the fact that the latter depends for its efficiency upon the patient's respiration, which is inhibited at this stage (when the patient is coming out). Respiration is quiet. The pulse is increased, as during ether inhalation, but apparently not so much. The blood-pressure, taken at ten-minute intervals, does not show a rise in proportion to the amount of liquid injected.

The following objections to the method might be raised: (1) Infection. Any careful operator should be able to eliminate this. (2) Embolism. Gas embolism is prevented by the use of the separating device, and the possibility of volatilization after entering the blood-vessels is reduced by the admixture of unsaturated blood-plasma, thus reducing the vapor tension. Blood-clot embolism from clotting of blood in the cannula when solution is not flowing may be obviated by a little care in washing out the cannula occasionally. (3) Overfilling of the circulatory system. The author's observations did not show any marked increase of intravascular pressure. (4) Hemolysis. No hemoglobinuria was observed and blood examinations did not reveal laking of the erythrocytes.

The series of cases operated by the author included the following major operations: Extensive **repair of male perineum, decompression, panhysterectomy, epithelioma** of the **lip** with plastic work, **brain tumor,** and **hernia.** L. W. Jenkins (Northwest Med., Dec., 1912).

Advantages of intravenous general anesthesia emphasized. The preliminary stage of excitement is nearly always absent, the respiration is almost natural, the color of the skin remains good, and the relaxation and flexibility are entirely satisfactory to the operator. The degree of narcosis can be maintained exactly, and when the operation is finished the patient is almost if not quite rational. The anesthetics used by the authors are varied: a 5 per cent. solution of ether, with filtered, sterile, **normal saline solution** at 85° F. (29.4° C.); **hedonal** dissolved in normal saline solution at 70° F. (21.1° C.) to make a 0.75 per cent. solution; **paraldehyde,** 2.5 per cent., and ether, 3 per cent. in normal saline solution; or paraldehyde alone. Ether always raised the blood-pressure 2 to 20 mm., while with hedonal it fell 10 to 12 mm. One case, purposely selected, with a blood-pressure of 186 mm., dropped to 142 mm., and remained at that level for some hours. There were no evidences of hemolysis beyond that usually occurring in ordinary saline transfusion, or in the respiratory administration of ether. As far as the blood-picture is concerned, hedonal is well borne. Complete anesthesia occurs in from one and one-half to twenty-three minutes with ether; with hedonal, in from twelve seconds to four minutes. Honan and Hassler (Med. Record, Feb. 8, 1913).

At the end of the operation, unless it has been very long, the dressing should be applied before the flow of ether is stopped, as the return to consciousness often comes very promptly (Honan and Hassler).

RECTAL ANESTHESIA.—Pirogoff called attention to this method of anesthesia in 1847. In 1884 Mollière took it up again. Finally, in 1904, Krougiline used it in 43 patients, and since that time greater interest in it has been awakened. It seems to possess inherent disadvantages, however, such as difficulty of management, tendency to irritate the rectal mucous membranes, and the possibility of death through rupture of a previously unrecognized intestinal ulcer, which will probably preclude its frequent use, especially in the face of the precise intratracheal and intravenous methods more recently introduced.

Description of a method of inducing ether anesthesia by rectum. A bottle, 7½ inches in height, of which 5 inches are used for ether space and 2½ inches for vapor space, is used. A tube penetrating the cork, and reaching nearly to the bottom of the bottle, is connected by means of a rubber tube with a cautery bulb. The efferent tube, which penetrates through the cork into the open space above the ether, is connected with the rectal tube. The bottle is placed in a water bath at 80° to 90° F. (26.7° to 32.2° C.). The patient lies on the back with the legs in slight flexion. The rectal tube is inserted from 10 to 14 inches, and the vapor forced in by pressing the cautery bulb. Keeping the forefinger in the rectum beside the tube, unless it causes the patient pain, hastens expulsion of the rectal gases. The rectum must be distended to the point of emptying itself around the tube, otherwise ether is absorbed much more slowly. After all the gas has been expelled the ether should be forced in by a few squeezes of the bulb every five or ten seconds. The breath becomes ether laden in from one to five minutes after the ether is started. When narcosis is complete, the usual precautions of ether anesthesia must be observed. If too great narcosis has taken place, the efferent tube should be disconnected, and ether be forced through the rectal tube by abdominal massage. Little ether is needed, vomiting seldom occurs, bronchial secretions are absent, and there is rapid recovery from the ether. Cunningham (Boston Med. and Surg. Jour., Sept. 12, 1907).

The advantages of rectal etherization are so great in operations on the face, mouth, neck and thorax that it deserves the preference in these cases. Irritation of the bowel can be avoided by blending the ether with **oxygen,** at body temperature, and preceding the application by a brief inhalation of **ethyl bromide** to relax the ileocecal valve. With this technique, general anesthesia by rectum is no more dangerous than by inhalation, unless the intestines are diseased. The author uses a Y-tube, one branch conveying the oxygen alone, the other branch passing it through a flask of ether, and the two branches then uniting in a single tube which conveys the mixture into the bowel. The oxygen and ether are rapidly absorbed and there is no meteorism as when air is insufflated. The anesthetic vapor should be introduced slowly. When the operation is completed, the rectal tube should be disconnected and as much as possible of the ether expelled with the aid of abdominal massage. Rectal narcosis has some contraindications—bad or doubtful conditions of the intestine, acute or chronic affections of the abdomen, operations upon the perineum or genital organs. It is not superior to the other methods in operations on the extremities, but does offer advantages in operations on the **face, neck, mouth,** and upon the **thorax.** It is a method to be used only exceptionally. Legueu, Morel and Verliac (Arch. gén. de chir., July 25, 1909).

Description of an apparatus for rectal anesthesia consisting of an outer jar (a galvanic cell) containing an ether bottle, the intervening space being filled with water at 90° F. (32.2° C.). Through the rubber cork is passed a long glass tube connecting with an ordinary cautery bulb, while a second perforation in the cork is occupied by a short tube providing for the exit of ether vapor. Between the bottle and the rectal tube is introduced a T-tube for the rapid relief of tension within the bowel or the attachment of an oxygen supply. Eberts (Montreal Med. Jour., Feb., 1910).

The colonic method of administering ether is more complex than the pulmonary method in general and requires from the anesthetist a broader appreciation of the physiological factors involved. It is a valuable addition to the armamentarium of the trained anesthetist. The indications are: **Operations on** or about the respiratory tract, especially such as lay open the **mouth, larynx, pharynx,** and **trachea;** when ether absorption must be minimized on account of lung, heart or kidney lesions; respiratory embarrassment. The contraindications are lesions of the alimentary tract, especially such as might cause weakness of the wall of the colon; laparotomies in general, except such as do not open the general peritoneal cavity, *e.g.,* suprapubic cystostomy; markedly incompetent sphincter or large, complete *fistula in ano;* orthopnea; emergency cases in general, because of the lack of preparation of the colon. Sutton (Annals of Surg., April, 1910).

LOCAL ANESTHESIA WITH ETHER.—Local anesthesia may be obtained by means of a spray of ether, which, through its rapid evaporation, causes intense cold and deadens sensation locally. This is a useful procedure for minor surgical operations, especially for the opening of **abscesses.**

While the more rapidly acting ethyl chloride is now used far more frequently than ether, it is a fact that the induction of local anesthesia with the former often causes much pain through the rapid freezing of the tissues induced. The slower action of ether renders it superior to ethyl chloride in this single respect, viz., absence of sharp preliminary pain.

OTHER USES OF ETHER.—As a **stimulant** in emergencies, *e.g.,* in **shock** and in **collapse** in **chronic heart disease** or in **acute infectious diseases,** ether is possessed of marked value. Hypodermic administration of 10 to 15 minims (0.6 to 1 c.c.)—or more in strong adults—is not infrequently followed by prompt reaction. One-half to 1 dram (2 to 4 c.c.) of Hoffman's anodyne may instead be given, either by mouth or hypodermically. The effect of ether on the heart and medulla is only of short duration, and should be supported with other stimulants. Its injection causes pain, and at least a part of the stimulating effect must be ascribed to the sensory impulses conveyed to the centers from the irritated peripheral tissues. A solution of 1 part of camphor in 5 of ether is sometimes administered subcutaneously for stimulant purposes.

> Ether found to be a good antidote of **cocaine** and **stovaine poisoning.** It should be administered as ordinarily given to produce surgical narcosis. It stimulates the heart and the respiratory system almost instantly. The pulse becomes fuller at once and of normal tension. The marked mental excitement is allayed. The anesthetic should be administered only to the degree of mild surgical narcosis, or, at times, even less than this. A mask should be employed and the ether given by the drop method. Engstadt (Jour. Amer. Med. Assoc., March 19, 1910).

As a Carminative ether may with advantage be used internally in disorders attended with **flatulence** and distention, in order to stimulate the muscles of the alimentary tract and assist in the expulsion of gas. Relief from **colicky pains** may simultaneously or independently be secured. The drug may be given either in the form of Hoffmann's anodyne (spiritus ætheris compositus), in doses of ½ to 2 drams (2 to 8 c.c.), or, less pleasantly, in the simple spirits of ether, the dose of which is the same. Ether is also occasionally given as such, in doses of 15 or 60 minims (1 to 4 c.c.), either in ice-water or cracked ice, on a piece of sugar, or in capsules. It forms a clear solution with 10 parts of water.

As an "Antispasmodic" ether is sometimes useful in disorders in which some part or other of the nervous system is overexcited, *e.g.*, in **hiccough, asthma** and other spasmodic neuroses, in **chorea,** in **hysteria,** and even in **migraine.** Thirty to 80 minims (2 to 5 c.c.) of ether in ice-cold water or in capsules, followed by a mouthful of water, are not infrequently promptly effective. Hoffmann's anodyne is often substituted for the pure ether.

W. W. Babcock administers the following combination by rectum when inducing mixed drug anesthesia (with morphine, scopolamine and apomorphine):—

℞ *Compound spirit of*
ether .... ℥j (30 c.c.).
Alcohol .... ℥ss (15 c.c.).
Normal saline solution,
enough to make.... ℥v (75 c.c.).—M.

To be slowly run into the bowel after the second injection of ⅙ grain (0.01 Gm.) of morphine and 1/100 grain (0.0006 Gm.) of scopolamine.

C. E. de M. Sajous
and
L. T. de M. Sajous,
Philadelphia.

ETHYL ALCOHOL. See Alcohol.

ETHYL AMINOBENZOATE

is the ethyl ester of paraminobenzoic acid. It is an odorless, tasteless, white, crystalline powder, very slightly soluble in water, but soluble in alcohol, ether, benzene, and fatty oils. It is decomposed by boiling or by the action of dilute alkalies. The drug is not official.

PREPARATIONS AND DOSE.—Ethyl aminobenzoate (*æthylis aminobenzoas*) may be used as a dusting powder, in ointment or in the form of suppositories. Internally it may be given in the dose of 5 to 8 grains (0.3-0.5 Gm.).

PHYSIOLOGICAL ACTION.—This drug is a local anesthetic, similar in its action to orthoform, and used as a substitute for cocaine. It is said to be as efficient as orthoform, but free from an irritant or toxic action. Being practically insoluble, it cannot be given hypodermically, and its anesthetic action is purely local, but more prolonged than that of cocaine.

THERAPEUTICS.—Locally, ethyl aminobenzoate may be applied as an anesthetic in **nasal** and **laryngeal diseases.** It is also said to be of value in **urethritis.** It may also be used locally in **wounds, burns, ulcers,** and painful **skin diseases.** Internally it has been given for the relief of pain in various forms of **gastralgia,** and in **gastric ulcer** and **carcinoma.** H.

ETHYL BROMIDE (*æthylis bromidum*).—Ethyl bromide, or hydrobromic ether, is an anesthetic prepared by combining bromine with alcohol in the presence of phosphorus. It was discovered by Sérullas, a French chemist, early in this century. It is an extremely volatile and colorless liquid, sweetish to the taste, and possessing an alliaceous odor. It is insoluble in water, but readily soluble in alcohol and ether. It presents the advantage over ether in not being inflammable. It is decomposed by sunlight and contact with the air.

Ethyl bromide is quickly eliminated from the system, and its after-effects are slight. Another preparation—ethylene bromide—is frequently dispensed instead of the bromide of ethyl; it causes nausea when inhaled, and in no way possesses the qualities of the latter. Ethyl bromide is, however, quite frequently found impure in the shops, and to this cause are due many of the untoward results met with.

PREPARATIONS AND DOSE.—Bromide of ethyl cannot be used for prolonged operations, owing to its high volatility. The dose, which varies with the age of the patient, should not exceed 6 drams (24 c.c.), 45 minims to 3 fluidrams (3-12 c.c.) being sufficient to induce anesthesia. For children, the dose should not exceed 16 minims (1 c.c.) per year of age. It should be administered rapidly with little or no air. The administration of bromide of ethyl should not be prolonged beyond two minutes.

The operation may usually be begun twenty seconds after the first inhalation.

PHYSIOLOGICAL ACTION AND UNTOWARD EFFECTS.—The dominant action of bromide of ethyl is said to be on the respiratory system, acting as a depressant, but only when given in excessive doses does it cause dangerous symptoms. It also lowers blood-pressure to a slight degree and slows the pulse, the latter being due to its action on the inhibitory nervous mechanism of the heart.

This drug frequently leaves a garlic-like taste in the mouth and gives a similar odor to the breath, but it rarely produces other disagreeable symptoms.

It causes death by arresting the heart's action, and the cases should be watched as if chloroform were being administered,—respiration and pulse simultaneously. The preliminary preparations for its administration are the same, and the recumbent position obligatory under all circumstances. Arrest of the heart may be caused, however, through vasomotor influence originating in an intoxication by compounds formed in the system.

> Two cases of ethyl bromide poisoning occurring in workmen engaged in the making of the drug. The noteworthy symptoms were sudden weakness and giddiness, along with disturbances of vision and dyspnea. With more severe poisoning or in more easily affected persons, psychic disturbance, possibly reaching to frenzy combined with delirium, occurred. It is remarkable that the most violent symptoms did not occur till the lapse of some days in the worst case. Experiments on rabbits with the drug showed diminution of spontaneity, gradual loss of power, then marked slowing, and, lastly, paralysis of respiration with epileptiform convulsions. The heart and vessels were affected very late. These experiments agreed with observations on men, in so far that the poisoning process did not cease with cessation of the inhalation, as is the case with other gas-forming poisons—*e.g.,* ether, chloroform, ethyl bromide—but continued to increase in intensity, and the animal died several hours after stoppage of the administration. Jaquet (Deut. Archiv f. klin. Med., Bd. lxxi, Hfte. 4-5, 1901).

Rules for the use of ethyl bromide: Do not use ethylene bromide. Do not use an old or impure solution. Do not administer it in repeated and small quantities. Give *en masse;* admit no air. Do not continue its administration longer than one minute. Another essential to success in the use of ethyl bromide in these operations is that the operator shall be quick in his work, and, in order that this may be true, a small and accurate instrument must be used. A. R. Solenberger (Jour. Amer. Med. Assoc., April 18, 1903).

Deaths from the use of the bromide of ethyl appear to have occurred chiefly some years ago before the sources of danger were understood. No death has been reported since 1897. The rapid anesthesia produced by bromide of ethyl, its short duration, the quick return to consciousness, and the absence of unpleasant effects are very striking. The majority of the deaths reported have been due either to excessive dose or to impurity. It should be administered by means of a mask covered with impermeable cloth, so as to exclude the air. Unsuitable persons are young children and those suffering from anemia, Bright's disease, fatty degeneration, and alcoholism. Vomiting occasionally occurs.

One drawback of bromide of ethyl anesthesia is that the muscles do not usually become relaxed. In mouth operations a gag should be inserted before the operation is begun. (Huggard.)

THERAPEUTICS.—Ethyl bromide is best used in short operations, as opening **abscesses** and **boils,** and may also be used in **chorea, epilepsy,** and other spasmodic diseases.

Montgomery has used ethyl bromide for anesthetic purposes in **labor,** and minor **gynecological operations.** As the drug does not cause uterine relaxation, post-partem hemorrhage is less likely to occur after its use.

The writer has used ethyl bromide in **dentistry** in 15,032 extractions, and considers it the best anesthetic to employ for these cases. Owing to the spastic condition which usually develops, the patient should be firmly tied to the chair and a suitable mouth-gag should be inserted before anesthesia is begun. A preliminary examination of the heart is often necessary to quiet the patient. From 10 to 20 c.c. (160 to 320 minims) of the anesthetic are then poured on a folded napkin and placed over the patient's face, so that he can inhale sufficient air before the narcosis is complete. It is not necessary to pay much attention to the pulse or corneal reflex, as the first signs of too deep anesthesia will be cessation of respiration and cyanosis.

It is important that a pure preparation be used and that this be kept well stoppered. It is often difficult to determine the proper moment for operating, but it is usually not necessary to wait for complete relaxation.

Among after-effects, vomiting is less common than after chloroform, and occasionally urine and stool are passed. The patients recover rapidly, and can generally go home without assistance.

The reason why ethyl bromide has not become more popular is probably because impure preparations are often employed. Breitbach (Merck's Archives, Oct., 1910). S.

ETHYL CARBAMATE. See Urethane.

ETHYL CHLORIDE.— Chloride of ethyl (monochlorethane) is a gas at ordinary temperatures, but which, when compressed, becomes a colorless, very inflammable liquid, boiling at 54.5° F. (125° C.). When ignited it burns with a green flame. It has an aromatic, sweet taste and an ethereal odor. It is exceedingly volatile, which latter property renders it unfit for anything but ephemeral anesthesia. This property causes it to evaporate so rapidly from the skin when applied locally in the form of spray that the cutaneous temperature is lowered sufficiently to become insensitive. Hence its employment as a local anesthetic.

DOSE AND PHYSIOLOGICAL ACTION.—For internal use it has been given in doses of 10 to 60 drops dissolved in an equal quantity of alcohol. Accordingly 5 c.c. (75 minims) should never be exceeded. When thus taken it has a stimulating action. When ethyl chloride is inhaled its chief effect appears upon the circulation and respiration, there being a marked lowering of the pulse rate and the blood-pressure; the respirations are at first increased in depth and frequency. Its action resembles that of chloroform. Large doses cause cessation of cardiac and respiratory movements.

Sprayed on skin or mucous membrane, it causes them to become white, cold, and insensitive by the process explained above.

> After an experience of 620 cases, the writer has satisfied himself that arterial tension, as a rule, is lowered during the administration of ethyl chloride, but that the pulse during deep narcosis becomes rather slower than normal and usually preserves its regularity. Respiration is markedly stimulated both in frequency and depth during deep anesthesia; the color is improved, due to vasomotor dilatation, which sometimes results in sweating and in one instance gave rise to a well-marked rash, like the ordinary ether rash. Adults as well as children take ethyl chloride very well and quietly, and very quickly pass under its influence. Any trouble during induction usually occurs with hysterical people, drinkers, smokers, and strong men. When excitement takes place, it is due to the too free admission of air, and yet at the same time a free use of air should be allowed. Failure of the anesthetic is also traceable to the too free mingling of air with the vapor. McCardie (Lancet, April 4, 1903).
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> In the open method of ethyl chloride administration the drug enters the system gradually and with free admixture of air; the shock given is more in the nature of a gentle push into unconsciousness as against the more violent and rapid rush into a state of insensibility in the closed method. With the open method there is no feeling of suffocation or desire to fight for air. It has been noticeable that there is very seldom any headache or feeling of great fullness in the head after the open method, both of which conditions are common after the closed. Ethyl chloride is very rapidly eliminated from the system, so that a few minutes after the completion of the operation the patient is quite fit to go home, a great advantage from the patient's standpoint as against ether or chloroform. Vomiting is rare unless the patient has swallowed some blood, in which case it will be brought up, but the nausea soon passes away.
>
> The writer does not recommend ethyl chloride for cases of more than five or ten minutes' duration, as it would be very expensive and has no advantage over open ether when prolonged anesthesia is required. In the whole of his experience of open ethyl chloride, either by itself or as a preliminary to open ether anesthesia—that is, in nearly 3500 cases of all ages, both sexes, and nearly every major or minor operation—he asserts he has not once had a moment's anxiety or had to resort to any artificial means of respiration. He thinks this fact is mainly due to absence of sudden concentration by the open method, and the feeling in the patient's mind that there is nothing to struggle against—he knows that he will not be suffocated, but will get air the whole time. Hornabrook (Austral. Med. Gaz., Nov. 20, 1911).

POISONING BY ETHYL CHLORIDE.—Ethyl chloride inhaled in toxic doses produces poisonous effects similar to those of chloroform, but it is less of a cardiac depressant. Death results from paralysis of the respiratory centers and the heart. According to H. C. Wood, Jr., the statistics seem to indicate that, as regards mortality results, ethyl chloride stands between ether and chloroform, but this conclusion he regards as unfair. The anesthesias by ethyl chloride have practically been all of but a few minutes' duration, and the prolonged anesthesias, which have to be credited with many of the fatalities of chloroform and ether, do not here come into consideration. The comparison should be rather with nitrous oxide gas. If we compare the commonly accepted mortality for nitrous oxide, 1 death in 1,000,000 anesthesias, with the figures for ethyl chloride, 1 in 6000, the danger of the latter is evident.

Ethyl chloride as a general anesthetic stands, as regards its mortality, next to chloroform, giving 1 death in 2075, ethyl chloride 1 death in 2550. In the writer's fatal case, the patient, a large and muscular man, became suddenly very much cyanosed; respiration gradually ceased, though the pulse was still perceptible at the wrist, and in spite of restoratives death occurred. At the *post mortem*, eccentric hypertrophy of the heart, with fatty degeneration of the heart muscle, marked arterial sclerosis of the coronary arteries, and slight sclerosis of the aorta were found. Also, the heart and veins were filled with fluid blood, and there was edema of the lungs. Lotheissen (Münch. med. Woch., May 1, 1900).

The writer collected from the literature 22 cases of death under anesthetization with ethyl chloride. Some of the cases were very bad subjects for any anesthetic. No less than 8 occurred during dental operations. Ethyl chloride is not a drug to be recommended off-hand, but requires, for its safe administration, discrimination, caution, and skill. In dental work it should not be given alone, but either in mixture with nitrous oxide in small doses for short cases, or in sequence with ether for longer cases. Luke (Lancet, May 5, 1906).

In 104 cases of ethyl chloride anesthesia, the duration of the anesthesia varied from one minute to fifty-five minutes, which time was that of a hemorrhoid case. In those cases in which deep anesthesia was induced, nausea was as prevalent as would have been the case with chloroform. When it was given only to the primary stages, as for most operations, there was none or at most but little. Of these patients 15 were babies, several of the operations being circumcisions of from ten to twenty minutes' duration; 35 patients were children, 50 were adults, and 4 were quite aged. The only alarming results encountered were in 1 case, that of an old man with pronounced arteriosclerosis and subject to asthmatic attacks. He showed a marked cyanosis with unconsciousness for about one-half hour, which cleared up under a hypodermic injection of 1/75 gr. (0.0009 Gm.) of **atropine sulphate.** Manwaring (Jour. Mich. State Med. Soc., Nov., 1906).

Case in which when surgical anesthesia was obtained there were clonic spasms of the legs and arms; respiration ceased, and the muscles of the jaws and neck were set in clonic spasm; cyanosis was marked; the eyes were fixed and staring, but the pupils remained contracted. Vigorous attempts to restore respiration were successful after there had been an actual suspension of respiration for about three minutes. Rugh N. Y. Med. Jour., vol. lxxxvi, p. 262, 1907).

The author has largely discontinued the use of ethyl chloride because it increased the coagulability of the blood; in consequence of this pulmonary embolism occurred, after the use of the ethyl chloride-ether sequence, more frequently than when ether was preceded by nitrous oxide. The frequency of such cases—at any rate at St. Thomas's—had coincided in time with the introduction into common use of ethyl chloride. Z. Mennell (Brit. Med. Jour., Mar. 16, 1907).

Ethyl chloride was used alone in 947 cases with ether in 4148, and with various other anesthetics in the remaining cases. The youngest patient was 24 hours old, the oldest 84 years old. The fatalities were 5, all of them occurring when ethyl chloride was used alone. The fact that the ethyl chloride was given first and in all the cases in which the patients were considered bad anesthetic risks distorts the statistics. Three deaths occurred under ether during its administration alone in 1444 cases. The facts that ethyl chloride can produce deep anesthesia in from fifteen to twenty seconds, and that its danger signs are so easily overlooked, are emphasized. In alcoholics and some others it produces muscular spasm and rigidity. W. E. Lee (Annals of Surg., Nov., 1908).

Ethyl chloride has a large margin of safety, but the danger signs are not marked. While it is very safe when administered by an expert, it may be very dangerous in unskilled hands. With an expert administrator, it should be safer than ether, but less safe than nitrous oxide. With an unskilled or careless administrator, it is probably more dangerous than ether, but not as dangerous as chloroform. Miller (Boston Med. and Surg. Jour., May 20, 1909).

Case of collapse under ethyl chloride general anesthesia in a boy of 7 years. The collapse occurred during removal of adenoid vegetations, with enlarged tonsils, and came on in half a minute. There was considerable hemorrhage, but the child was revived by artificial respiration. Nielsen (Ugeskrift f. Læger, April 11, 1912).

Treatment of Poisoning by Ethyl Chloride.—When poisoning has been induced by the inhalation of ethyl chloride, the tongue should be drawn forward, and caffeine, strychnine, or atropine given by hypodermic injection. Artificial respiration should be used faithfully, the head being lowered as in chloroform syncope. Amyl nitrate, ammonia, and warmth are also useful.

Although the writer used ethyl chloride in 3000 anesthesias, he has never had a mishap. But he always supplements the ethyl chloride with chloroform or ether for a long operation. None of the mishaps attributed to ethyl chloride bear investigation, with the exception of 1 case in which the patient was given 150 minims (10 c.c.) of ethyl chloride within three minutes. As the respiration stops first and the heart keeps on beating for a time, artificial respiration should be the first measure applied in case of asphyxia, with possibly massage of the heart, and the patient will be promptly restored, as the extremely volatile drug escapes from the body very rapidly. Herrenknecht (Münch. med. Woch., Dec. 3, 1907).

THERAPEUTICS. — In general practice the great convenience of ethyl chloride is such as to recommend it for minor or short operations such as removing tonsils, adenoids, opening abscesses thoroughly, removing toe-nails, scraping sinuses, and other small operations requiring one minute to a minute and a half.

Ethyl chloride is the best anesthetic known for single-dose cases, those in which anesthesia is induced, the mask removed, and the operation performed without further administration. While its effects are transient it is a powerful anesthetic and should be carefully administered, and the patient properly prepared.

While for an adult of the ordinary type nitrous oxide is the best, for certain operations on the eye, mouth, and nose which cannot be satisfactorily performed under non-continuous gas anesthesia, ethyl chloride either alone or combined with gas has proved a valuable addition to the measures at the command of the anesthetist. In operations for enlarged tonsils and adenoids, where the chloroform mortality is exceptionally high, ethyl chloride is the best anesthetic. For single-dose cases in adults, except in case of big, muscular men, the writer prefers the nitrous oxide and ethyl chloride mixture. Equally as good results can be obtained with smaller doses of ethyl chloride as when the drug is administered by itself. The mixture is an ideal anesthetic for cases requiring anesthesia of from forty seconds to two minutes.

There is no advantage in continuing the administration of ethyl chloride after the first few minutes of anesthesia. It is more difficult to keep up a level type of narcosis with ethyl chloride than with either ether or chloroform, the extreme volatility of the drug making it difficult and irksome to administer methodically. The writer feels less confident of the safety and rapidity of ethyl chloride as a preliminary to chloroform and ether. Some of the deaths and untoward results which have occurred under the ethyl chloride administration may have been due to too large dosage, and hence are preventable. J. H. Chaldecott (Clinical Jour., Aug. 1, 1906).

Ethyl chloride in **operations on the throat** in children is very satisfactory. It does not require to be given to deep anesthesia, and the child is soon able to arouse sufficiently to cough all material out of the throat and larynx. The author has performed over 1000 operations on the throat in children. There have been no postoperative hemorrhages, but infection has in a few cases caused sore throat, stiff neck, and fever. Ethyl chloride is very easy to give on a few thicknesses of gauze over the inhaler. The patient is quickly under the influence and quickly comes out. E. M. Sill (Med. Record, Oct. 23, 1909).

The most striking feature of ethyl chloride is the rapidity of its action. The patient is unconscious usually in forty-five seconds, and it is a mistake to keep the inhaler on longer than fifty to sixty seconds. It is possible to **amputate** a finger or toe during one administration of ethyl chloride. The stitches, however, may have to be deferred until the patient has recovered his senses (Lytton Maitland).

Ethyl chloride is not generally recommended for infants, but it is the best means of procuring short anesthesias of from five to fifteen minutes in children of any age. It appears to be as safe for babies as for older children, and it does not produce bad after-effects. The writer has administered it to 150 infants under a year old. The youngest cases were 5 and 14 days respectively, and a large proportion of them were from 5 to 7 weeks old. They included a number of weak and ill-developed children, common to hospital out-patient departments. It is useful in **tenotomy, sounding, circumcision,** and the **removal of adenoids, lipoma,** or **polypi.** For most such operations an anesthesia of ten or fifteen minutes is sufficient. Infants suffer less from the after-effects of the drug than adults. F. Murray (Lancet, Nov. 25, 1905).

The author administers the anesthetic in three stages and anesthesia should be present at the end of the second. In the first stage the patient inhales C. E. mixture from the mask, the quantity varying from 1 to 3 drams, according to age and physique. After a little time, varying from half a minute to one and a half minutes, he sprays ethyl chloride, from 3 to 7 c.c. (45 to 105 minims), and applies the towel closely over all. This is the second stage. It ends with the loss of the corneal reflex, generally lasting from a quarter to one and a half or two minutes. The towel is now removed, and the third stage entered on. It consists simply in maintaining a proper degree of anesthesia by means of the C. E. mixture or chloroform. A little judgment and practice soon enable one to steer the middle course, and, without overdosing, to give patients enough of the anesthetic to prevent any return of consciousness. A spasm of the jaw, more or less marked, occurs during the second stage. By watching the jaw during the third stage the writer believes that one has a valuable guide to the depths of anesthesia, as the spasm gradually passes off under the influence of chloroform. So long as it remains, no matter what other symptoms are present, one may feel sure that the patient is not getting too much chloroform. The author states that he now adopts this method as his routine practice, finding that it saves time, does not unduly alarm nervous patients, and suits children admirably. Barton (Practitioner, Sept., 1907).

Anesthesia by ethyl chloride, used from a 50 c.c. (1⅔-ounce) tube of glass is advocated. For each five seconds that the container is open with the nozzle downward, 1 c.c. (15 minims) will escape into a rubber bag, from which it is inhaled. Oil of sandalwood will lessen the disagreeableness of the odor. R. H. M. Dawbarn (Med. Rec., May 22, 1909).

The legitimate field of usefulness of ethyl chloride lies in the production of local anesthesia for the relief of pain and for the purpose of performing minor surgical operations in dental surgery.

Local Anesthesia.—Ethyl chloride is usually dispensed in large tubes, one end of which is drawn out to a fine point, or in tubes closed by an automatic cap. When the former are used, the point is broken off, and the tube held in the hand, at a distance of from six to ten inches from the part to be anesthetized. The heat of the hand causes the liquefied gas to issue in spray-form. By its rapid vaporization the part soon becomes frozen and ready for operation. As the skin hardens under the ethyl chloride the exact limits of the operation must be determined beforehand. The highly inflammable nature of this agent must be remembered, and operations must be done at a good distance from gas and other flames or by electric light. The absence of unpleasant after-effects and of any influence on the sensory centers of the brain are its advantages over some other agents used for local anesthesia. It is used in the treatment of **ingrowing toe-nails,** the **opening of abscesses, removal of ganglia,** or for any painful skin incision. If the liquid is ignited as it issues from the broken tip, the flame thus produced may be used to cauterize septic or aseptic wounds or for cutaneous cauterization.

Neuralgia.—Ethyl chloride in spray has been used with success in **supra-orbital** and **facial neuralgia, sciatica, neuralgia** of the **breast,** upon the painful joints of incipient **gout,** scrotal **pruritus** (diabetic), and in **migraine.** From 2½ to 5 drams (10 to 20 c.c.) may be used in spray at one sitting, the lesser quantity usually being sufficient.

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Philadelphia.

ETHYL NITRITE. See Nitrites.

EUCAINE HYDROCHLORIDE

(beta-eucaine hydrochloride) is a synthetic substance approximating cocaine as to its chemical formula. It is termed beta- or B- eucaine to distinguish from alpha-eucaine, an earlier but less valuable substance proposed by the originator of both, Vinci. The free base of beta-eucaine is nearly insoluble in water, but it combines with acids to form soluble salts, one of which is the hydrochloride.

PREPARATIONS AND DOSE.—*Eucaine hydrochloride* is employed in lieu of cocaine to produce local anesthesia. The strength of the solution to be used depends upon the locality to which it is applied. A 2 per cent. solution is strong enough to produce anesthesia of the eye, while a 5 to 10 per cent. solution is required for mucous membranes. Stronger solutions can be used, however, without fear of producing toxic phenomena. It forms a permanent 3½ per cent. solution in water, and may be boiled without being altered. Solutions stronger than this can be obtained by warming (Braun).

> In nose and throat anesthesia solutions of different strength were tried by the writer in various **operations on** the **nose** and **throat.** He considers that it may, unlike cocaine, be used in the strongest solutions without fear of toxic symptoms. It does not lose its anesthetic power under the usual periods of office use. Its anesthetic effect seems to be somewhat less than that of cocaine, and in the more painful operations should be used in correspondingly stronger solutions. Thos. J. Harris (Laryngoscope, June, 1905).

Eucaine hydrochloride is also used in *infiltration anesthesia.* The procedure is as follows: Powders are kept in stock in the operating room containing 0.02 Gm. (3 grains) of beta-eucaine and 0.8 Gm. (12 grains) of pure sodium chloride. At the time of the operation one such powder is dissolved in 100 c.c. (3⅓ ounces) of boiling distilled water, and when it is cooled sufficiently 1 c.c. (15 minims) of adrenalin chloride solution (1: 1000) is added; 100 c.c. (3⅓ ounces) of the resulting liquid contain 3 grains (0.2 Gm.) of B-eucaine and 0.015 grains (0.0009 Gm.) of adrenalin chloride. The whole 100 c.c. (3⅓ ounces) may be used at one infiltration anesthesia, but according to Barker from 50 to 60 c.c. (1⅔ to 2 ounces) usually suffices, even in such considerable operations as for the cure of hernia and castration. It is, of course, essential that the syringe used be aseptic, and the surgeon should always employ the platinum needle with an iridium point which can, without injury, be disinfected in the flame of an alcohol lamp immediately before use (H. C. Wood, Jr.).

Eucaine lactate is much more soluble than the hydrochloride and is employed when strong solutions (5 to 20 per cent.) are required. When local ischemia is desired epinephrin (1: 1000) is added to the solution, as indicated under the heading of THERAPEUTICS.

PHYSIOLOGICAL ACTION.—The manner in which eucaine hydrochloride produces anesthesia is not clearly established. It does not cause constriction of the arterioles as does cocaine, but paralyzes the sensory terminals without causing irritation or injury to the tissues. A weak solution suffices to produce an anesthesia of sufficient duration to render minor operations possible, while stronger solutions render more serious operative procedures painless. A valuable property of eucaine hydrochloride is that it can be boiled without losing its anesthetizing property.

Internally, eucaine hydrochloride was found by VerEecke to produce the following effects:—

In the frog it determines successively excitations, convulsions, and paralysis; the latter is of peripheral origin. The return to the normal state is accompanied by convulsions, and later by hyperexcitability. The fatal dose is 0.16 Gm. (2½ grains) per kilogram (2⅕ pounds). In the warm-blooded animals it produces excitation, which is followed by convulsions and, finally, death from asphyxia. There is no paralyzant dose. The fatal dose in the guinea-pig is from 0.049 to 0.052 Gm. (¾ to ⅞ grain) per kilogram (2⅕ pounds). There is no cumulative action of the poison; on the contrary, the organism may accustom itself to increasing doses of the drug. Cocaine has twice the toxic action which is possessed by eucaine. Eucaine hydrochloride acts on the heart principally by paralyzing the intracardiac motor center and secondarily it alters the muscular fiber of the heart. It lowers the blood-pressure by diminishing the peripheral resistance. It directly stimulates the respiratory center in the medulla. The paralysis of this center which occurs in fatal poisoning is not the result of the direct action of the poison, but is due to asphyxia, which in its turn is caused by an excess of carbon monoxide in the blood. It increases diuresis, accelerates nitrogenous, phosphorous, and chlorous metabolism, and produces glycosuria, but only during the presence of intense convulsions. It does not appear to be eliminated by the kidneys; on the other hand, it probably undergoes a chemical decomposition in the body. Instilled in the conjunctival sac eucaine hydrochloride first produces anesthesia of the conjunctiva and, finally, of the cornea at the same time that it rapidly lowers the intraocular pressure. It reduces the vitality of the red blood-corpuscles and produces fatty degeneration of the heart and of the involuntary muscles.

POISONING BY EUCAINE.—Intoxication by this agent is extremely rare, a great advantage over cocaine (*q.v.*). Kraus (Deut. med. Woch., B. xxxii, No. 2, 1906) witnessed a case in a robust, phlegmatic man of 40 years, on whom internal urethrotomy had been performed the day before, under local anesthesia with 10 c.c. (2½ drams) of a 2 per cent. solution of eucaine hydrochloride.

The injection was repeated the next day when he came to have the cut stricture stretched. Almost at once he felt faint and became partly unconscious, with increasing dyspnea, distress and chills, while the breathing grew shallower and shallower. The conditions lasted in all for an hour or an hour and a half. The patient was able to eat then, but did not sleep much that night and found that he was somewhat forgetful for a day or so afterward. There was no actual collapse. Treatment was with **wine** and **camphor, faradization** of the phrenic nerves in the neck and inhalation of **oxygen.** It was the first time that any mishap has been observed from the use of beta-eucaine in Lewin's Urologic Polyclinic, although it is in daily use there.

Two cases of intoxication from eucaine hydrochloride have also been reported by Marcinowski. In 1 case the patient had a transient syncope, but she was subject to fainting. In the other case, after injection of 1.5 c.c. (23 minims) of a 10 per cent. solution the patient exhibited tonic and clonic spasms, which gradually subsided after fifteen minutes, but were followed by stupor and weakness, the symptoms all passing away by the end of six hours. Dolbeau reported a similar case after intravenous injection of eucaine hydrochloride, and Simon has mentioned transient headache and vomiting in a man whose bladder had been filled with 80 c.c. (2⅔ ounces) of a 4 per cent. solution for a Bottini operation.

Treatment of Eucaine Poisoning.—The inability of eucaine to produce contraction of the peripheral blood-vessels, and the physiological effects of its internal use tend to suggest that the phenomena of intoxication are due, in oversensitive individuals, to paresis of the vasomotor terminals as well as that of the sensory terminals. Stimulation is therefore indicated. Besides **oil of camphor** injections, inhalations of **oxygen** and **faradization** of the phrenics were employed successfully by Kraus. **Epinephrin solution** (1:1000), 20 drops in saline solution intravenously, suggests itself as the most efficient measure, owing to the specific stimulative action upon the arterioles.

THERAPEUTICS.—For *local use,* eucaine lactate is preferable owing to its greater solubility and the fact that stronger solutions are required than for infiltration anesthesia. Harris (Amer. Med., Dec., 1905), with a 10 to 15 per cent. solution, was able to perform septal and other serious nasal operations. To sustain the effect he added epinephrin, as shown in the following formula:—

℞ *Eucaine lactate.*	0.52 Gm.	(8 grains).
Sodium chloride.	1.40 Gm.	(21 grains).
Distilled water..	52.00 c.c.	(14 drams).
Adrenalin chloride sol.......	1.00 c.c.	(16 minims).

This was applied on cotton for ten minutes. When a septal or a serious operation was to be performed he injected 20 to 30 minims (1.3 to 2 c.c.) of the solution at two or three points in the septal mucosa, thus avoiding all pain.

> The writer uses a 12 per cent. solution of lactate of beta-eucaine to anesthetize the mucous membrane in nose, throat, and ear troubles. It does not disturb the circulation or shrink the tissues, hence in operations on the turbinals the amount of tissue which should be removed is easily estimated. For **turbinotomy** he uses a 12 per cent. solution on a cotton tampon, which is allowed to remain five minutes, and is then replaced by a fresh one, which

remains a similar time. A 5 per cent. solution dropped into the conjunctival sac causes more smarting than a 4 per cent. solution of cocaine, but there is neither hyperemia nor anemia, and vision is in no way disturbed. The anesthetic effect is equal to that of a 4 or 5 per cent. cocaine solution. H. B. Ellis (Calif. Med. and Surg. Reporter, March, 1905).

Judging from his experience with beta-eucaine which extends over ten years, the writer prefers this anesthetic because it can be sterilized, does not irritate, and invariably produced a most complete anesthesia and causes less toxic manifestations than like agents, when used in an equal strength or quantity. In fact, when beta-eucaine is employed in ⅛ per cent. solution in **anorectal operations,** the patient rarely complains of pain or dizziness or turns pale, becomes excited or faints during or following the operation. This is partly due to the non-toxic effect of the drug, and partly to the fact that the solution is very weak and escapes during or following operation. S. G. Gant (Merck's Archives, Nov., 1910).

For **infiltration anesthesia** eucaine was found by Barker and many others to possess analgesic properties little, if at all, inferior to cocaine. One hundred c.c. (3⅓ ounces) of a fluid containing 0.2 per cent. beta-eucaine, with epinephrin, can be used in an ordinary case if necessary, and is quite sufficient for most operations. Twice as much may be injected without ill results. The duration of the insensibility is secured by the admixture of epinephrin. Without it sensation is only abolished by eucaine for about fifteen minutes; with it, for three or four hours. But the analgesia is produced more slowly when epinephrin is employed. It is therefore well, before all larger operations, to wait some thirty minutes after injection to allow time for the insensibility to become fully developed. After this the effect appears to deepen for a couple of hours. Waiting has another advantage, in that by the time operation is begun the artificial edema has disappeared and details are very clearly seen. Rapid injection is to be avoided; sudden distention of the tissues is disagreeable, if not painful. The fluid should not be used cold nor too hot, for the same reason. All dragging on the parts is to be avoided, lest structures be pulled upon which lie beyond the area of infiltration.

Various authors have failed to see depressing effects follow the use of beta-eucaine in a long series of operations, including **abdominal sections, hernia** operations, **amputations, orchidectomy,** removal of **cyst of thyroid,** removal of silver wire from around the patella, operations for **fistula in ano, varicose veins, hydrocele, varicocele,** etc.

The area of infiltration of the skin should be made directly in the line of the proposed incision and should be long enough to allow of easy exposure of the tissue beneath. When the operation is to extend into the deep tissues it is best to infiltrate step by step and not to attempt to infiltrate the whole tissue at once. Among the operations performed under his anesthesia were **partial thyroidectomies** for **exophthalmic goiter; ligation of arteries;** radical operations for **malignant disease of the breast; gastrostomies; gallstone operations; appendectomies; renal decapsulation; nephrectomy; nephrotomy; hysteropexies; myomectomies;** radical **inguinal** and **umbilical herniotomies; perineal cystotomies, operations for hallux valgus.** Witherspoon (St. Louis Med. Rev., Mar. 24, 1906).

Eucaine has also been used to obtain spinal anesthesia, but its indications for this purpose will be considered under the heading of SPINAL ANESTHESIA. W.

EUCALYPTUS. — Eucalyptus U. S. P. is the leaves from the older parts of the *Eucalyptus globulus labilliardiere.* The eucalyptus, or blue-gum tree, is a tall, evergreen tree, a native of Australia, but now grown all over the world. From the leaves the oil of eucalyptus is obtained by distillation, and from this oil, by redistillation with caustic potash or calcium chloride, a camphoraceous body is obtained which is known as *eucalyptol*. The latter is the refined product.

It was once thought that, as the tree grew easily in marshy districts and drained the soil of water, it would diminish the malaria miasm of low, swampy regions, and in that way prove a prophylactic against malaria. Laveran has shown, however, that the organism causing malaria troubles is, in all probability, taken into the body through the media of food and drink, and that the planting of the eucalyptus trees does not diminish the paludal fevers. The prevailing view that mosquitoes are the main intermediaries through which the infection occurs also tends to diminish faith in eucalyptus as a prophylactic, though the tree itself tends to keep these pathogenic insects away.

The leaves have a camphoraceous odor and a pungent, bitter taste, and yield a volatile essential oil, the oil of eucalyptus, which is the active principle. Eucalyptus oil is a faint-yellow, sometimes colorless liquid, having a characteristic aromatic odor and a pungent, cooling taste, and being soluble in alcohol and in bisulphide of carbon. The value of the oil depends upon the amount of eucalyptol present.

Eucalyptol is a colorless liquid, with a strong, aromatic, camphoraceous odor; is slightly soluble in water, but easily soluble in alcohol, ether, and fatty oils.

By treating oil of eucalyptus with hydrochloric acid Anthoire has obtained a white, micaceous, scaly substance, hygroscopic in nature, called eucalypteol. It is soluble in alcohol, ether, chloroform, and oils, but almost insoluble in water and in glycerin. It is not poisonous, and is tolerated by the stomach.

PREPARATIONS AND DOSE.—*Eucalyptus,* ½ to 2 drams (2 to 4 Gm.).

Extractum eucalypti fluidum (fluid extract of eucalyptus), 10 drops to 2 drams (0.6 to 8 c.c.).

Oleum eucalypti (oil of eucalyptus), 5 to 20 minims (0.3 to 1.25 c.c.).

Eucalyptol, 1 to 15 minims (0.06 to 1 c.c.).

Eucalypteol, 24 grains (1.5 Gm.) daily, in divided doses.

PHYSIOLOGICAL ACTION.—Applied externally, the oil is a decided irritant, and causes heat and redness of the part, due to dilatation. When inhaled it causes an increase of the saliva and of the bronchial secretion. When taken internally in medicinal doses it produces a feeling of warmth and stimulation, with increased secretions, while larger doses are productive of disordered digestion, diarrhea with loose stools having the characteristic odor of the oil, and symptoms of renal and cerebral congestion. When larger doses are used there are noticed a rapid, weak pulse, general excitation, and restlessness; decrease of body heat, lower arterial pressure, irregular and weak respirations; muscular weakness, especially of the lower limbs; and death from respiratory paralysis. The drug is eliminated by the bronchial mucous membranes, the skin, the kidneys, and the bowels. The urine may have the odor of violets, as noticed after the ingestion of the oil of turpentine. The oil of eucalyptus, like most aromatic oils, is an antiseptic and a germicide, and in sufficient strength it inhibits the growth of micro-organisms in culture media. Eucalyptus is a powerful diuretic. An increased excretion of urine is said to follow its internal use.

POISONING BY EUCALYPTUS.—Tonic doses of eucalyptus give rise to the symptoms of gastrointestinal irritation, renal and cerebral congestion, impaired circulation, muscular weakness and paralysis, and finally death by respiratory failure. Cases of poisoning are not frequent.

> Case of poisoning in which between 2 and 3 teaspoonfuls of oil of eucalyptus had been swallowed. The severe stupor, myosis, and hypothermia which followed suggested opium poisoning. Stertorous breathing, however, was absent. Recovery. F. C. Wood (Brit. Med. Jour., Jan. 27, 1900).

> Case of eucalyptus oil poisoning. A boy, 6 years of age, who had occasionally been in the habit of getting a drop or two of eucalyptus oil on sugar, was given by mistake a teaspoonful of the same. This was about 6 o'clock one evening. About 8 he had his usual light supper, and within two hours thereafter abdominal pain and severe vomiting set in. The vomiting continued without cessation of any length and diarrhea soon became marked. By 11 o'clock the boy became drowsy, and when he was seen about this time he was semicomatose. He was pale and collapsed, with a small but not very quick pulse. The muscles generally were flaccid. The pupils were medium in size and equal. The conjunctival reflex was not quite abolished. The tendon reflexes were present and were not exaggerated. There was no cough and the breathing was shallow. He could be roused by very vigorous slapping of the face, but each time he looked dazed. Every time he was wakened up the sickness and vomiting set in. The vomited matter, which consisted of mucus and watery material, had a strong smell of eucalyptus oil. After two or three hours of external stimulation very much along the lines usually adopted for opium poisoning, the heavy comatose condition appeared to pass off, and the child was allowed to sleep. He slept well and next morning, beyond being a little tired, was quite himself again. The breath had a smell of eucalyptus oil for three days. There was never any irritation of the urinary tract. The poison showed itself by gastrointestinal irritation and cerebral paresis. Foggie (Brit. Med. Jour., Feb. 18, 1911).

Treatment of Poisoning by Eucalyptus.—In mild cases the gastrointestinal symptoms should be ameliorated through the use of **morphine, bismuth, lime water,** etc. In severe cases, when the circulation and respiration are profoundly affected, the use of **caffeine, strychnine,** and **atropine** by hypodermic injection is advised.

THERAPEUTICS. — Eucalyptus has a selective action upon the mucous membranes, being excreted through them. To them it is a stimulant, antiseptic, germicide, and antispasmodic, and we find that its most beneficial action is exerted, therefore, directly upon the gastrointestinal tract, the bronchial tubes, and the genitourinary tract; indirectly upon certain mucous disorders more or less dependent upon the integrity of tissues and function of those organs. In general, it is contraindicated in acute inflammatory conditions. The tincture has been found very useful in the treatment of **hemorrhages** of various kinds.

> The writer highly recommends the application of the tincture of eucalyptus for the arrest of any form of **hemorrhage.** He mentions 3 cases in which all means to stop the persistent hemorrhage failed, but the bleeding ceased immediately upon the application of the tincture of eucalyptus. One

case was that of a boy, who had a tooth extracted three days before, and had persistent hemorrhage from the socket. Another case was that in which there was profuse hemorrhage from the cut in the patient's foot, and in the last case the hemorrhage followed the application of a leech to the gum. He also calls attention to the use of this preparation as a dressing on lint after circumcision or other minor operations. A. Todd-White (Brit. Med. Jour., July 11, 1908).

Gastrointestinal Disorders. — In **atonic dyspepsia** and **chronic gastric** or **intestinal catarrh**, eucalyptus is one of the most useful stomachics. In **convalescence** from acute disease and in **debility from defective assimilation** it is a useful stimulant and tonic. In the **flatulence, cardiac palpitation**, and **hot flashes** of the **menopause** it is often of permanent benefit. It has been found useful in **cholera**, 5 minims (0.3 c.c.) being given in milk every quarter-hour for one hour, then every hour. On account of its antiseptic action, eucalyptus oil and eucalyptol have been used in **typhoid fever**, being administered in capsules.

Bronchial Disorders.—In **subacute** and **chronic bronchitis** eucalyptus loosens the secretions, stimulates and gives tone to the mucous membrane, and exerts, withal, an antiseptic action, especially in cases accompanied by free mucopurulent secretion. It is also useful in **bronchorrhea**. Oil of eucalyptus, in ointment suitable for inunctions, has recently been tried in **pulmonary tuberculosis**. The method seems worthy of trial.

The method of use is to direct that 1 teaspoonful of the preparation be thoroughly rubbed into the skin until it disappears, varying the locality with each application. The following formula was employed:—

℞ *Olive oil*	℥ij (60 c.c.).
Benzoinated lard..	℥vj (180 c.c.).
Cacao butter	℥iv (120 Gm.).
Eucalyptus oil	℥iiiss (105 c.c.).

This amount contains 15 minims (1 c.c.) of eucalyptus oil, the major part of which reaches the circulation. In many instances the constitutional effects have been noted after one application. The most striking early effect was a change in the character and quality of the expectoration: having been yellow, viscid, and moderate in volume, it froths up and becomes white, free, easy to expectorate, and temporarily more abundant. Then follows a reduction in the amount of sputum, accompanied as a general rule by a continued improvement in the cough.

Coincidently with these changes, the temperature ran a lower and more favorable course, the change usually beginning within twenty-four hours of the first administration. The patient generally reports a feeling of well-being which is known to be one of the characteristic effects of the drug. L. G. Pedigo (Therap. Gaz., March 15, 1913).

Genitourinary Disorders. — In **chronic cystitis, pyelonephritis**, and **chronic desquamative nephritis** eucalyptus has been recommended as an efficient remedy. In **subacute gonorrhea** Hare advises 6 minims (0.36 c.c.) each of eucalyptus oil and sweet-almond oil in a capsule after meals.

Malaria Fevers.—Eucalyptus has been praised as a remedy for **intermittent fever**, in the absence of quinine or where idiosyncrasy interdicts its use. It cannot take the place of quinine to arrest the paroxysms, or to prevent relapses at the septenary periods, but is more useful than quinine to reconstruct the damages in the organs of assimilation caused by malarial infection.

Nervous Disorders. — **Spasmodic asthma** is much relieved by eucalyptol given by steam inhalation. Cigarettes made from eucalyptus leaves alone, combined with stramonium, belladonna, tobacco, etc., give similar relief. **Pertussis** has been relieved by a mixture of 1 part each of eucalyptus oil and terebene, and 6 parts of alcohol, used in spray half an hour before meals and at bedtime (Hardwicke). **Malarial or congestive headache** may be relieved by oil of eucalyptus, 5 minims (0.3 c.c.) being given four or six times daily.

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EUDOXIN is a compound of iodine, bismuth, and phenolphthalein. It is a tasteless, odorless powder, having a reddish-brown color. It is insoluble and contains about 60 per cent. of iodine. The drug is not official.

PREPARATIONS AND DOSE.—Eudoxin may be given in the doses of 5 to 20 grains (0.3 to 1.3 Gm.) to adults. It may also be used as a dusting powder.

PHYSIOLOGICAL ACTION.—Locally, eudoxin acts as an astringent and a protective. Internally, the drug acts as an intestinal antiseptic and antifermentative.

THERAPEUTICS.—Locally, eudoxin is used in **burns** and **ulcers**, and has also been found of some value in certain skin diseases. It has also been used in some eye diseases. Castor oil, containing enough eudoxin to make a thick paste, may be found of value as a local application for **cracked nipples.**

Internally, eudoxin is of value in catarrhal inflammations of the bowels. It is also recommended in the **diarrheas** of children.

H.

EUMYDRIN is the nitrate of methylated atropin. It is a white, crystalline, odorless salt, slightly soluble in ether or chloroform, but readily soluble in water or alcohol. It is incompatible with alkaline solutions. The drug is not official.

PREPARATIONS AND DOSE.—Externally, eumydrin may be used in a 1 to 2 per cent. solution to produce mydriasis. It may be given internally in the dose of 1/60 to 1/24 grain (0.001 to 0.0025 Gm.).

PHYSIOLOGICAL ACTION.—Eumydrin is a mydriatic and antihydrotic. It has been used in place of atropine, as it is said to act more rapidly and to be less toxic. Its effects wear off more quickly than when atropine is used. It is claimed that eumydrin has the peripheral action of atropine without its effect on the central nervous system.

THERAPEUTICS.—Eumydrin may be used locally in the eye to produce **mydriasis.** Internally, it is said to be of especial value in the treatment of **pertussis, night-sweats,** and **enuresis.**

> Eumydrin is useful in functional and secretory neuroses of the alimentary tract, such as **hyperchlorhydria, gastralgia, intestinal spasm, perityphlitis,** etc., and in all conditions of the stomach and intestines in which belladonna or atropine is indicated. Eumydrin is much less toxic than atropine. Its dose is 1/60 to 1/15 grain (0.001 to 0.004 Gm.) three or four times a day, and it may be prescribed in pill, powder, solution or suppository. G. Haas (Therap. der Gegenwart, Nu. 3, S. 105, 1905).
>
> Upon healthy and diseased irides, it acts, in equal doses with atropine, more slowly, with less energy, and its effect is not so lasting; on the other hand, it is less toxic and appears to have no influence upon the tension. It can be substituted for atropine in children, the aged, and when the latter is not well borne. In 0 5 per cent. solution it acts more rapidly than homatropine, but its effects last about ten hours longer; this can be decidedly shortened by pilocarpine, rendering eumydrin preferable when, for examination, dilatation of the pupil is desired. Del Monte (Arch. d. ophthal., July, 1906). H.

EUONYMUS, or Wahoo, is the dried bark of the root of *Euonymus atropurpureus,* a plant of the United States. It occurs as curved or quilled pieces having a pale brownish-gray or ashy outer surface, and a whitish or light-brown, smooth inner surface. There are small, dark, scaly patches over the external surface. It has a distinct odor and a slightly bitter and somewhat acrid taste. It is slightly soluble in alcohol or ether, and freely soluble in water. Euonymus contains a bitter, amorphous substance known as *euonymin,* atropurpurin, and several acids.

PREPARATIONS AND DOSE.—The average dose of euonymus is 7½ grains (0.5 Gm.).

Extractum euonymi, U. S. P. (extract of euonymus), is made by the evaporation of the fluidextract and the addition of powdered glycyrrhiza. Dose, 2 grains (0.125 Gm.).

Fluidextractum euonymi, U. S. P. (fluidextract of euonymus), is made by the maceration and percolation of the drug with alcohol and water, followed by evaporation. Dose, 8 minims (0.5 c.c.).

PHYSIOLOGICAL ACTION.—Small doses of euonymus act as a tonic, increasing the appetite and the gastric secretions. It is a direct cholagogue, and a slow and mild laxative.

The drug has also been credited with some expectorant and diuretic action, and first increases and then decreases the excretion of uric acid. Large doses act as an intestinal irritant.

THERAPEUTICS.—Euonymus is useful in all hepatic derangements and is also used in **indigestion** and chronic **constipation.** It is also claimed to be of value in **malaria** and **dropsy.** H.

EUPHTHALMINE HYDROCHLORIDE is a colorless crystalline powder derived from beta-eucaine and is soluble in water.

PREPARATIONS AND DOSE.—Euphthalmine hydrochloride is used in a 5 to 10 per cent. solution, 2 or 3 drops of which may be instilled into the eye.

PHYSIOLOGICAL ACTION.—Euphthalmine is a prompt mydriatic. It has no anesthetic action, and does not produce any pain, irritation of the cornea, or increase in intraocular tension. The effect of euphthalmine disappears more rapidly than that of atropine. Its effect on the general system resembles atropine.

THERAPEUTICS. — Euphthalmine is used as a **mydriatic** in ophthalmoscopic examinations in place of atropine. The fact that its effects are relatively ephemeral, constitute an advantage when but a single examination under a mydriatic is necessary.

The value of euphthalmine as a brief **mydriatic** is now well established, all observers being fully agreed regarding it. There is also complete agreement as to its freedom from danger of any injurious effect upon the cornea, such as strong solutions of cocaine are likely to produce. Regarding the risk of producing an outbreak of glaucoma with euphthalmine, while it is probably less than with any other mydriatic but cocaine, and most writers speak of it as *nil,* we must remember that every other new mydriatic has been put forward with the same assertion, but experience has in each case failed to substantiate the claim. Jackson and Schneideman (Amer. Jour. Med. Sci., June, 1900).

In many cases of **cataract,** central opacity of the lens precedes cortical involvement. If the pupillary aperture be narrow, as is generally the case in the aged, vision is greatly interfered with by such central opacity, which blocks the entire pupil, and where the condition is bilateral, the patient is unable to read or write. The operation of preliminary iridectomy usually performed under these circumstances may be impossible for two reasons: 1. General disease contraindicating operation. 2. Refusal of the patient to be operated. For several years the author has successfully used in these cases euphthalmine hydrochlorate, which, by its mydriatic effect, permits of vision through the uninvolved cortical portions of the lens. A mydriatic used for such a purpose must be shown to be entirely harmless, since it may have to be used for several years. In the use of euphthalmine the author has observed no untoward effects. Intraocular tension is not affected, accommodation is but rarely and very slightly influenced, and there are no secondary intoxicating effects. Sometimes there is a slight burning sensation of the conjunctiva in the first half minute after use. Mydriasis begins in twenty minutes and lasts four hours with the 3 per cent. and seven hours with the 5 per cent. solution. To avoid the dazzling effect from the increased admission of light, the patient's ordinary glasses may be colored blue or greenish yellow. The drug must not be used after 6 P.M.; 1 or 2 drops after breakfast enable the patient to read in the morning, and 1 or 2 at noon, in the succeeding afternoon hours. With this procedure persons previously debarred from all work may, in part at least, resume their former occupation. A. Dufour (Revue méd. de la Suisse Romande, Jan. 20, 1910).

H.

EUQUININE. See CINCHONA.

EUROPHEN.—Europhen, or iododiisobutylorthocresol, is the result of the action of iodine on isobutyl alcohol and orthocresol with zinc chloride by heat. It is allied to aristol and appears as a light, dull-yellow, amorphous, aromatic powder, which is soluble in alcohol, ether, chloroform, and oils, but insoluble in glycerin or water. It has an aromatic odor, like saffron, but has no taste. It is stable when kept dry. On prolonged exposure to moisture it is decomposed, setting free nascent iodine. If heated to 158° F. (70° C.) in the presence of water it is decomposed; hence heat should not be employed in making solutions of it. It contains 28.1° of iodine. It was introduced as a substitute for iodoform. Europhen is incompatible with the metallic oxides, all preparations of mercury, and starch.

DOSE AND PHYSIOLOGICAL ACTION.—Internally the dose is 1 to 3 grains (0.065 to 0.2 Gm.). By hypodermic injection (in a 3 per cent. to 10 per cent. solution in olive oil) the dose is 1 to 1½ grains (0.065 to 0.1 Gm.) once daily. Externally, it is used in 5 per cent. to 10 per cent. ointment, dissolved in olive oil or lanolin (5 per cent. to 30 per cent.), as a dusting powder (1 part to 3 of boric acid), in 10 per cent. gauze, or pure.

The therapeutic value of europhen depends upon the liberation of iodine when it is exposed to moisture. In this its action is similar to that of iodoform; but europhen parts with its iodine more slowly, even under the most favorable conditions; and while it is thus less poisonous than iodoform it is also, for the same reason, less efficient.

On the other hand, it is more bulky, will go farther, and is less likely to cake than iodoform. Its properties are those of an antiseptic, antisyphilitic, and alterative. It exerts a polyseptic action upon bacterial growth.

THERAPEUTICS.—Europhen is not generally given by the mouth, although it has been administered in **syphilis**, in doses of ½ to 2 grains (0.032 to 0.13 Gm.). It is not considered poisonous; as much as 23 grains (1.5 Gm.) has been taken daily for three weeks without any appreciable disturbance. It is believed that europhen taken internally passes through the bowels almost unchanged. The hypodermic use of europhen has not met with much favor, and, although tried in the treatment of syphilis, it has not yielded the results anticipated. As a surgical dressing and in some **cutaneous disorders**, principally those presenting moist or secreting surfaces, europhen has found great favor.

Europhen has been highly recommended by Flick in the treatment of **pulmonary tuberculosis.** He introduces it into the body by means of inunctions, using the following formula:—

℞ *Europhen* .... ʒij (8 Gm.).
Oil of roses .... ♏ij (1.2 c.c.).
Oil of anise,
Oil of gaultheria,
of each .... fʒij (8 c.c.).
Olive oil, enough to
make .... f℥v (150 c.c.).

The quantity to be used is proportionate with the age of the patient.

Wounds.—In recent wounds of traumatic origin europhen has proved of great usefulness, showing a high efficiency as an antiseptic dressing. Marked drying powers without local irritation and absence of odor are the principal advantage of europhen over iodoform. All kinds of wounds heal quickly under it. It has been used with great success after superficial operations, such as removal of skin tumors, circumcision, and cauterization. In postoperative fistulæ it has been found better than iodoform. **Erosions, fissures,**

and **sinuses** may be dusted with europhen and then covered with 10 per cent. europhen gauze.

Cutaneous Disorders.—In skin affections of a dry or scaly character europhen is inactive, as might be inferred. In dry eczema, favus, and psoriasis its value is slight. As a dusting-powder in the **intertrigo** of children it has found great favor. In **pustular eczema, folliculitis, impetigo, suppurating lupus,** and **scrofuloderma** europhen has proved of equal value with iodoform. In **scalds** and **burns** and **erysipelas** it is of considerable service, a dressing of 3 parts of europhen in 7 parts of olive oil being suggested. In **chronic, indolent ulcers** and in **leg ulcers** with a surrounding eczematous area europhen soothes the burning and itching, and allays the pain, whereas iodoform is irritating. **Boils** and **carbuncles** are dressed successfully with europhen. In the treatment of tubercular growths europhen is inferior to iodoform.

Venereal Disorders.—Europhen is a valuable dressing for **balanitis, chancroids, suppurating buboes,** and **phagedenic ulcers,** as well as for **tertiary syphilitic conditions affecting mucous surfaces,** or with a moist or secreting surface. Europhen may be applied, as in other surgical cases, in powder, ointment, oily solution, or in the form of gauze, as the nature of the case requires.

Nasal Disorders.—In **atrophic rhinitis, ozena, septal ulceration** (syphilitic or traumatic), and in **postoperative wounds** of the **nasal cavities** europhen is very valuable, as it adheres well to the mucous membrane, is devoid of unpleasant odor, and has marked antiseptic and healing powers.

Ophthalmic Disorders.—Pick (1910) found europhen valuable in **septic diseases of the eye,** particularly when these occur as a result of local injury, foreign bodies, etc. He evacuated the pus and introduced europhen into the organ. W.

EXALGIN—Exalgin (methylphenylacetamide, or methylacetanilid) is prepared by warming together monomethylaniline and acetyl chloride. It occurs in acicular needles, which are with difficulty soluble in cold water, more readily in warm water, and more easily in dilute and concentrated alcohol. It is odorless and tasteless.

DOSE.—Exalgin may be given to adults in doses of 2 to 4 grains (0.12 to 0.25 Gm.) every two to four hours. A maximal daily dose of 15 grains (1 Gm.) should not be exceeded. According to Bardet the doses of exalgin, as set forth in the formularies, are too high. The maximum dose for twenty-four hours should be, for a man, 4 grains (0.25 Gm.), and for a woman, 2½ grains (0.16 Gm.). Children from 1 to 12 years of age may be given ½ to 1½ grains (0.032 to 0.1 Gm.) three times daily. Owing to its pleasant taste, it may be given dry on the tongue, in wafers, and dissolved in wine or water, to which a little alcohol has been added (exalgin, 1 part; alcohol, 1¼ parts; sweetened water, 125 parts).

Sodium salicylate added to exalgin increases its solubility for hypodermic use (exalgin, 10 parts; sodium salicylate, 11 parts; water, 100 parts). In short, the dose of exalgin is one-fifth that of antipyrin.

PHYSIOLOGICAL ACTION.—This is similar to that of acetanilid. It is capable of acting energetically upon sensibility and the motor-nerve system, and later upon the respiratory and circulatory systems. In tonic doses it acts upon the blood-corpuscles like all poisons of the same class and diminishes the activity of the gaseous changes therein. In animals, mortally toxic doses produce violent convulsions and insensibility; death is from asphyxia. In toxic non-mortal doses convulsions are observed. In man the temperature is not reduced except when exalgin is administered in small, repeated doses during several hours. It acts first upon sensibility; its action upon thermogenesis comes later and is accessory. With feverish patients untoward effects are accentuated; hence the presence of fever is a contraindication to its use. While large doses in animals do not produce albuminuria or hematuria (Brigonnet), in man the quantity of urine decreases, the color becomes darker, and urobilin and indican are present, if the dose is large. Arterial pressure occasionally falls slightly, though usually there is a rise, with a decrease in pulse rate. Vasomotor disturbances are indicated by free or profuse diaphoresis.

EXALGIN POISONING.—No fatal poisoning from exalgin has been reported, although serious symptoms have followed so small a dose as 5 grains (0.3 Gm.). In this case, an asthmatic, the effects of this small dose were noticed within five minutes. Unconsciousness was associated with shallow, infrequent, and failing respiration. The lips and finger-tips became cyanosed and the extremities cold; the pupils were fixed and widely dilated; knee-jerks were absent. Later an evident tendency to heart-failure. The urine could be drawn with catheter (secretion suppression). In other cases larger doses have produced numbness and tingling, vertigo, temporary blindness, tinnitus aurium, headache, profuse sweating, cyanosis followed by pallor, formication, etc. The brain seems to be the first organ affected and the first to recover. General motor paralysis with dyspnea, pallor, palpitation, and physical prostration were the symptoms in another case. There is sometimes a feeling of alternate expansion and contraction of the head.

> Case of an arthritic and hysterical woman, who took, for the mitigation of an attack of migraine, a cachet containing 4 grains (0.25 Gm.) of exalgin. This dose in a short time produced upon the skin and the mucous membrane of the anus and vagina a general papulose eruption, with patches of a fiery-red color, and, in certain spots, large blisters, containing a clear, serous fluid. The rash, which lasted four days, caused pain when pressure was applied, but it was not pruriginous. Linossier (Jour. de Pharm. et de Chim., No. 8, p. 413, 1898).
>
> Case of exalgin poisoning occurring in an adult male Chinaman. It was estimated that the dose taken was 150 grains (5 Gm.) of Merck's preparation. The patient when seen was quite unconscious, intensely livid, with pinpoint pupils and a full, bounding pulse. His temperature was 100.6° F. (38.1° C.). He had vomited once. He was given 30 grains (2 Gm.) of **salicylic acid** by a nasal tube and 1⁄50 grain (0.0013 Gm.) of **atropine** hypodermically, and was put to bed. Two hours later he was given 1⁄100 grain (0.00065 Gm.) of atropine, and a few hours later a third dose consisting of 1⁄100 grain (0.00065 Gm.). The urine contained albumin when first seen, but by the following morning the albumin had disappeared and the patient generally was much improved. Complete recovery ensued. J. Bell (Lancet, Sept. 30, 1899).
>
> A patient suffering considerably from headache and insomnia received ½ Gm. (7½ grains) of the drug in the morning; during the afternoon she complained considerably of palpitation of the heart and a feeling of oppression. After subsequent doses of the same size the distress became even more marked and was coupled with formication, vertigo, spots before the eyes, tinnitus, dilation of the pupils, increased pulse rate, and a pronounced cyanosis of the visible mucous membranes. After two days of active treatment with stimulants, warm baths, and diuretics, the symptoms had disappeared. That great care is to be exercised in the administration of exalgin is evident. O. Seifert (Wien. klin. Rundsch., June 29, 1902).

Treatment of Exalgin Poisoning.—The first indication in the treatment of poisoning is to evacuate the stomach. **Apomorphine** in doses of 1⁄10 to 1⁄6 grain (0.006 to 0.01 Gm.) may be given hypodermically for this purpose. Cardiac and respiratory stimulants (**ether, strychnine,** and **caffeine** by hypodermic injection, or **strong coffee by the rectum**) are then demanded. **Morphine** by injection may be given if there are convulsions or if much rigidity is present. If the respirations fail, **artificial respiration** should be kept up faithfully, and **faradization** of the **phrenic nerve, stimulants,** and **warmth** applied. In all cases of poisoning thus far reported, these remedies have been successfully used.

THERAPEUTICS.—Exalgin is essentially a remedy against pain, as its name indicates. It is an antineuralgic, antirheumatic, and sedative. It should never be given to patients suffering with any interference of respiration nor used as a means of reducing temperature, for experience has shown that in febrile cases the untoward effects of the drug are marked.

Used externally diluted, as a dusting powder, exalgin has been found to exert a slight anesthetic effect on painful **ulcers, burns,** and injured surfaces.

Exalgin is used to relieve the pain of **rheumatism, arthritis,** the various forms of **neuralgia, headaches,** and the lightning pains of **locomotor ataxia.**

Small night and morning doses (2 or 3 grains—0.12 or 0.2 Gm.) have been found useful in many cases of **epilepsy** and **chorea,** but in these disorders medication must be continued for several weeks to be successful.

In all cases exalgin should be administered in small doses until the susceptibility of the patient is ascertained; thus only will dangerous symptoms be avoided.

W.

EXOPHTHALMIC GOITER.

See Graves's Disease.

EXTERNAL EAR, DISEASES OF THE.—The external ear furnishes about one-fourth of all aural work, by reason of its diseases and anomalies; and in consideration of the fact that much of our examination and treatment of the middle ear has to be through this channel, its careful study is requisite in otology. Statistical tables show that more than half of these are cases of impacted cerumen, and the bulk of the remainder fall under the convenient—if vague—headings of diffuse, or eczematous, and circumscribed, or furuncular, inflammations; but the rarer affections have still enough of pathological interest to call for brief discussion.

MALFORMATIONS.—Many of the malformations of the auricle have only embryological interest; but the rudimentary microtia is usually accompanied by stenosis or absence of the auditory canal, and the question of operative intervention comes up,—generally for a negative answer. Possibly a crumpled auricle can be straightened out by plastic operation for more natural growth, and a covered bony canal can be opened; yet too often exploration fails to find the canal, and even the tympanum may be undeveloped; so any opening of the bone is contraindicated. Otherwise any reasonable **plastic surgery** may be attempted. The little *congenital fistula* seen at times above the tragus may suppurate and demand **curetting** or **excision,** and auricular appendages or reduplications of the auricle may call for **removal.** Bad malposition of the auricles may rarely justify **cosmetic operation.**

Prominent ears, in addition to being unsightly and a cause of mental suffering to the owner, are a source of physical danger in that they may deflect currents of cold air against a delicate drum membrane, especially on windy days. For this latter reason he suggests the desirability of changing the "set" of them. In his method of operation he excises practically all the fibrocartilage of the concha, antihelix, and antitragus. An ellipse of skin is removed from the posterior part of the ear and from the mastoid region of the scalp, of such a shape that one half relates to the ear and the other half to the mastoid region of the scalp. The cartilage is then removed, and the very thin skin over concha and antihelix is buttonholed at one or more points for purposes of drainage. The ear is then sutured in place, and two thicknesses of iodoform gauze cut to conform with the wound line are nicely fitted between the skin of helix and skin of scalp. Previous to **operation** the auditory canal is plugged with cotton which is removed, and the meatus left open, before the final dressings of iodoform gauze are applied. Morris (Med. Rec., March 23, 1912).

INJURIES.—Wounds, burns, frostbite, and abscesses (see FURUNCLE, below) should receive the usual surgical treatment, the last being rare except in the lobule, where generally due to septic piercing for earrings.

Two cases of infants with tubercular infection of the ear and enlargement of related lymph-nodes; one was 9 weeks old, the other 4 months. Both had had their ears pierced for the wearing of earrings, when a few days old, by the midwife. Eleven other cases of tuberculosis of the lobe of the ear, probably caused in the same way were found in literature. All had had their ears pierced in infancy. Epstein (Zeit. f. Kinderheilkunde, Aug., 1912).

Hematoma and perichondritis are often of traumatic origin, each marked by effusion between the perichondrium and cartilage with serious impairment of its vitality. Deformity is apt to follow; but early relief of tension and judicious use of massage are our best measures for cure or mitigation. Any inflammatory symptoms, such as usually differentiate these otherwise similar affections, are to be allayed before much stimulation is attempted.

In 2 cases the ear had been torn off. The writer cut a corresponding piece of cartilage from the costal arch and implanted it in a large skin-flap with the attached base above just below the clavicle. Later this flap containing the cartilage with the skin on each side was twisted around and sutured to the stump of the ear. The pedunculated flap was held in place by immobilizing the boy's arm over his head. V. Schmieden (Berl. klin. Woch., Aug. 3, 1908).

Case of elongation of the lobule of the ear following edema from acute nephritis, a hitherto undescribed disfigurement, for which he proposes the name "othygroma nephriticum." The writer believes there is some analogy between this condition and othematoma, but as the patient would not permit any operation or the removal of a piece of tissue for examination, the pathological conditions cannot be given. O. Glogan (Jour. Amer. Med. Assoc., Jan. 11, 1913).

GROWTHS.—Cysts are generally back of the ear and more commonly congenital, however late the apparent beginning. They may be serous, sebaceous, or teratoid, and should be dissected out entire.

Fibroma of the lobule is usually a keloid formation sequent upon piercing or the wearing of irritating rings; it is therefore commoner in the negro. It is not apt to attain great size and seems always benign; but thorough eradication is the only safeguard against prompt recurrence.

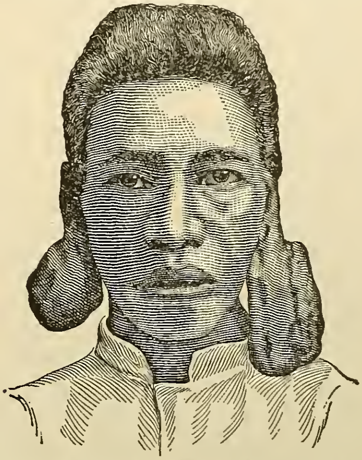
Other neoplasms are too rare to need special discussion.

Case of a girl, 12 years old, who complained of pain in both ear-lobes a year ago. They became swollen and abscesses formed. After the pus was drained off, a swelling remained on both sides which gradually changed into a circumscribed tumor resembling cartilage. The histological examination of a section of the extirpated tumors showed the picture of an enchondroma consisting of elastic cartilage. Zografides (Wiener klin. Woch., Jan. 2, 1913).

ECZEMATOUS INFLAMMATION of the auricle is commonly due to its extension from the canal, where it has been set up by irritating discharges. Intertrigo back of the ear or isolated affection of the pinna or canal has often other causes; and in the absence of otorrhea, gout, struma, or other malnutrition, is apt to be its basis. It may be a severe affection, with pyrexia and almost phlegmonous swelling, and in such cases it is wiser to isolate, give full doses of **tr. ferri chlor.**, and deal with it as erysipelatous. Locally there are generally abundant micro-organisms; and whether these are causative or not, we should, with all promptness, remove the conditions favorable to their growth. Moisture is to be avoided, as well as any oily materials which might decompose and irritate, and any weeping of the surface should be dried by vigorous use of **silver nitrate. Bismuth, calomel, hydrarg. oxidi flavi,** or **ichthyol in weak ointment** should relieve the irritable conditions—**oil of cade** or more stimulating salves, the more chronic phases. As a prelude to any treatment, the affected surface should be cleaned as perfectly as possible of all crusts or desquamation, **hydrogen dioxide**, especially in 60 per cent. alcoholic solution, being probably the best agent, since it also penetrates and disinfects, while bringing to view, as snowy patches, affected areas beneath the surface. The chosen ointment should then be rubbed in, gently but persistently, until these deeper patches have been again made invisible by its penetration. The prescribing of medication without supervising or personally carrying out the employment of it will generally prove ineffectual. It is safest to continue its use periodically for a month after all symptoms are past.

Eczema of the external ear is often stubborn at best and prone to recur, and **strict regimen** and constitutional medication may be requisite to ward off attacks. Herpes may, in very rare cases, be mistaken for it; but the pain in herpes is very apt to be severe before any eruption occurs, and the course of the affection is quite different.

The itching of eczema is as trying in the canal as in any other location, and there is a strong temptation to scratch, abrade, and infect the surfaces. Furuncle is apt to follow, and autoinoculation may establish a series. As elsewhere, there are two sets of glands open to involvement, the superficial sebaceous hair-glands and the deeper coiled glands, here secreting cerumen instead of sweat. The latter may actually enter the perichondrium or periosteum; so their suppuration may not only cause swelling of the whole aural region and displace the auricle in a way suggestive of mastoid abscess, but may really cause caries of the bony wall. Hence slight eczemas deserve treatment as a prophylaxis, even when no redness or desquamation marks their existence.


Fibrous tumors of the lobules. (*Bullard.*)

Induration is present in most chronic eczemas, and the resulting rigidity of the auricle and canal is often our only diagnostic sign. Something of this sort will generally be found in the other ear when one only is affected with furuncle. The right ear is more often affected in adults, probably as it is more often scratched.

FURUNCLE may be extremely painful and a series occurring in a patient out of health may positively endanger life through exhaustion. The first appearances should be vigorously treated, therefore, and the later stages sedulously cared for until resolution is complete.

> The differential diagnosis between the swelling back of the ear caused by furunculosis of the external auditory canal and swelling behind the ear from mastoid disease is very simple. In the former there is *edema* of the soft parts back of ear, and in the latter there is *infiltration*. In the one case (edema) the swelling pits on pressure and in the other (infiltration) it does not. In infants there may rarely be some edema in mastoid disease, but it almost never occurs in adults and is not so marked. N. H. Pierce (Laryngoscope, June, 1908).

The hearing is unlikely to be involved except temporarily; but the condition should not be too lightly regarded or the sufferer may seek a more sympathetic attendant. **Leeching** may greatly relieve the painful tension and abort or limit the lesion; **heat**, dry or by douche, is generally more convenient and as efficacious. The temperature should always be hotter than pleasant and the douche should be followed by drying, to avoid maceration. Poulticing is to be condemned, unless done for very brief intervals and only at the hottest bearable. Granulations about the mouth of an open furuncle are almost as certain evidence of abuse of poultices as is a "tea-leaf eye." Disinfection by mopping with **hydrogen peroxide** gives the benefit of massage, and should be followed by rubbing in of the **ointment of the yellow oxide of mercury.** This should not only be rubbed in vigorously, but be inserted on a conical wad of cotton wedged in as firmly as can be tolerated. If the patient will bear this for the first few minutes, it generally reduces the congestion and brings relief, and it can even be pushed in more and more so as to maintain pressure. A persistent inunction and massage are thus obtained at every motion of the jaw, and a canal that was wholly closed one day with a furuncle that threatened days of suffering may be found open and well on toward resolution next day. In the deeper form of the involvement such pressure cannot be endured. Heat will here have a limited value, and instillations of atropine, cocaine, morphine, carbolic acid, or a thousand vaunted remedies may avail as little. **Morphine** in full dose must be called in, therefore, to supplement the resolvent effect of **heat** by douche and hot-water bottle. Bags of salt retain heat well and can be used to good advantage, as can the Japanese hand-stove if its fumes are avoided. **Incision** of the swelled tissue, whether pus has formed or not, is in theory unimpeachable; in practice it can be generally avoided with moral and physical relief to the patient and an impression that the healing has been better without it. Diagnosis of the conditions beyond the swelling may be impossible, and tympanic involvement had better be assumed until it can be disproved; hence swellings in the bony canal, where glands are few and furuncle rare, should be earlier incised, and the possibility of underlying bone disease never lost sight of as a cause, rather than a consequence, of the visible lesion.

Six cases in which circumscribed otitis in the outer ear was treated internally with **yeast**, taken two, three, and four times a day. The tendency to recurring furuncles in the ear was promptly arrested and there has been no recurrence since. The patients took the yeast for about a week. This yeast treatment was supplemented by local application of medicated gauze. Under the influence of the yeast the pain and the morbid tendency rapidly subsided, although the furunculosis had long persisted unmodified by other measures. N. Antenore (Gazz. degli Ospedali e delle Clin., May 4, 1909).

A small pledget of cotton-wool is impregnated with equal quantities of **ichthyol** and **glycerin** and introduced into the meatus, followed by a second pledget of dry cotton-wool to prevent any of the solution running out. Care must be taken to prevent the pledgets from exercising any pressure, otherwise the pain would be increased. The application may be renewed once a day, or in very painful cases night and morning, and the treatment should be continued until the desiccation of the furuncle is complete. If the furuncle breaks, the cotton-wool impregnated with ichthyol prevents further infection of the meatus inward, and there is no fear of setting up eczema of the passage, such as not infrequently occurs with other moist applications or instillations of glycerin and carbolic. In cases in which it may be necessary to incise the furuncle the ichthyol application forms a suitable subsequent dressing. F. Bruch (Merck's Archives, March, 1910).

Few affections are so painful as an abscess in the outer ear, but it is possible to abort and cure it by the simple means of making three to five lengthwise **incisions** in the passage at the point where the pain is most severe. The writer does not wait for the abscess to ripen, but makes the incisions at once when the patient complains of pain. The meatus and outer ear are thoroughly disinfected to begin with; then the incisions are made where the probe shows that there is most painfulness. Then he covers the incisions at once with strips of gauze dipped in a 10 per cent. solution of **phenol**, with or without preceding application of **cocaine**. The phenol has an anesthetic as well as a sterilizing action, and it is absorbed promptly through the raw surface of the incisions. The pain subsides in the course of an hour or two and has entirely disappeared by the fifth hour. Zografides (Wiener klin. Woch., Dec. 19, 1912).

In acute otitis media and the extremely painful furunculosis of the auditory meatus, the writer recommends the following combination:—

℞ *Anesthesin* ...	1 Gm. (15 grains).
Alcohol absol.	10 Gm. (2½ drams).
Liq. alum. acetatis	2 Gm. (30 minims).
Glycerini	30 Gm. (1 ounce).

The solution is warmed and applied by saturating with it a sterile strip of gauze which is inserted up to the drum menbrane three to five times a day. The gauze is then moistened with the solution, while externally a Priessnitz dressing is applied.

The above formula or combination is very effectual and never causes any intoxication like cocaine or any cauterization like the popular 10 per cent. carbolized glycerin. For painful affections of the larynx, the author prefers a mixture of equal parts of anesthesin and iodol with 1 per cent. menthol, insufflated three times a day. Huebner (Therap. Monats., Feb., 1912).

GRANULATION MASSES may be found in the canal, arising from its wall. Unless fringing the opening of a poulticed furuncle, these generally mark a sinus leading to or into the bone. There may be a burrowing out of tympanic pus along the periosteum by a track which a bristle could hardly follow; but generally a fine probe will find its way to bare and carious bone. A superficial lesion should be laid open and **curetted**, as **cocaine** will generally enable us to do with sufficient vigor. A deeper lesion will belong to the field of middle-ear surgery.

INSPISSATED CERUMEN constitutes about one-seventh of the aural disorders. It is rarely a condition that can be regarded as merely an incidental retention of normal earwax, nor does the dirty occupation of even the coal-heavers, who are affected with it, more than partially explain its occurrence. There is generally more or less involvement of the middle ear behind it, and the *decreased* amount and greater consistence of the excretion is often, as in the pharynx, the reason for the apparent increase of its amount. Wax is generally wholly lacking in suppurating ears, although brownish, inspissated pus is easily mistaken for it; and in the chronic tympanic catarrhs it is generally a very good omen when wax begins again to form in the usually empty canal. Faulty configuration sometimes hinders its natural escape; but generally this is associated with an eczema which adds much exfoliated epidermis to the collection. The wax glands are situated only in the outer two-thirds of the canal; so any wax found deeper is a foreign body, generally pushed there by meddlesome attempts at its removal.

The healthy ear needs no artificial cleansing of its canal. Nature has provided that the epithelium of the center of the drumhead shall grow faster than at any other point; hence it tends to overgrow its surroundings, as it were, and, pushing the older cells before it, to creep along the canal wall. Superficial extravasations on the drumhead can thus be seen to migrate off its surface and a little way along the canal, before they are thrown off; and this outward growth carries all foreign material away from the tympanic membrane, where it might seriously impede function. Outside of the narrowed "isthmus" of the canal the wax glands are present, and one of the functions of the wax is doubtless to agglutinate the flaky material. The motions imparted by the jaw to the lining of the canal are then probably all that is needful to convey these particles to the exit,—the spring of the hairs upon which they get caught serving to throw them at times out upon the shoulder.

When, through defect of this natural cleansing process or artificial interference with it, collections form within the canal, they are commonly at the middle third and may fill almost completely this tube; but so long as the smallest crevice remains through which the sound-waves can reach the tympanum there may be no symptom of their presence. Pressure may be noted or other irritation lead to interference, and then the mass may be pushed down upon the drum or made to occlude the meatus. More often the entrance of moisture swells the hydroscopic mass, and sudden and complete closure of the ear, with deafness, tinnitus, and autophony, may alarm as well as distress the patient. Sudden deafness without pain or vertigo is apt to signify impacted cerumen.

The opposite ear is commonly in similar condition; so the habit of examining it first may save us from letting the same experience befall the patient there. A dark-brown or blackish, greasy mass can usually be seen at the first glance, even on drawing the canal straight and letting the light from a window fall into it past the examiner's head. Sometimes the hairs are enough to hide it and must be pressed aside with a speculum. This must here, as always, be used only under good illumination of the canal or it may serve to press the mass all the more distressingly. In all these examinations, as also in all manipulations in the canal, the normal configuration of the meatus must be borne in mind. It has an oval lumen with the longer diameter vertical at the exit, but inclining forward as we go in. Its axis is spirally curved and tends usually upward and forward as we pass in, but the floor seems to sink a little as we approach the drumhead, constituting a slightly broadened, deepened sulcus, out of which foreign materials are rather hard to remove. The soft parts constituting the outermost third of the canal exaggerate the curves and have to be drawn up (down, in the infant) and back and out in order to straighten it as much as possible, both for seeing in and for washing out anything there retained. The helix should therefore always be grasped between the index and middle fingers, so that this traction may be efficiently made, and yet the thumb and index tip be left free to manipulate a speculum or otherwise serve us.

Wax plugs and all other foreign bodies should be washed out with the **syringe.** Only where this has been fully and skillfully used without avail has the most expert a right to employ other instruments, and then only with a gentle, steady hand and on a quiet or etherized patient. In almost all cases the syringe is the most efficient as well as the safest and gentlest means at our command; but it must be better used than is common if it is to justify this claim. A small, smoothly working piston syringe is to be preferred, with a small tip that can enter a little way into the canal without obstructing the view. The fluid employed should be **hot water.** It matters little or not at all whether this is medicated; **soda, boric acid,** or any harmless drug may be dissolved in it if the surgeon believes it better than pure water. The best solvent is really heat, and a temperature of 110° to 115° F. (43.3° to 46.1° C.) is generally well borne and less apt to cause dizziness than "lukewarm" water. A cup of some sort should be held beneath the lobule and the shoulder covered with a towel; then with the canal well illuminated by the forehead mirror or other means and drawn straight as above described, we gently begin to inject the hot water. Perhaps along the upper back wall is the best direction for the stream; but this must be varied as sight of the mass suggests. Beginning gently, the first few drams serve to moisten the parts, the next to disintegrate the plug, discoloring the returning fluid with the dissolved wax; usually with my two-dram instrument the eighth syringeful washes the mass out into the cup, with an expenditure of 2 ounces (60c.c.) of water and five minutes, at most, of time.

But epidermis is not soluble in water or any other available material. When the impaction consists largely of laminated epithelium, especially if really a cholesteatoma mass working out from the middle ear, no such easy task is to be anticipated. Prolonged syringing, aided by skillful use of the probe and forceps, perhaps, must be employed to remove such a mass, and prudence may dictate adjourning the completion of the matter to a second sitting. The canal walls are often excoriated beneath such a mass, and exfoliating, but not yet fully detached, epidermis may anchor it to tender surfaces, from which it should not be violently torn away. But in true cerumen impaction there is little or none of this. Delay in soaking or otherwise trifling with the plug only increases any irritation from its pressure. The patient, if put off, may never return to the surgeon, whom he truly says made him worse instead of better. *Dizziness* or *fainting* may compel a suspension of the sitting; but if the patient has been warned to announce the first sensation of the sort, this can generally be forestalled, and an eye should generally be kept open for any clammy sweat on his brow. Pressure upon the tympanic structures is a common cause, and suction with the squeezed Politzer bag fitted in the canal or the palm laid over the ear will often undo the mischief and give instant relief. If not, the patient should be laid flat by tilting his chair back until the head is on or near the floor and be induced to lie still until feeling right again, when the chair can be raised again and we can proceed in a few moments without repetition of the disturbance.

After this and all other syringing, the canal should be gently dried with absorbent cotton on a delicate carrier and the air shut out by a light flake in the exit; otherwise there will be chilling from the evaporation of the trace of moisture left, with possibly unpleasant reaction. Any *excoriated surfaces* should be anointed or dusted with boric acid or aristol, and any needed treatment given to the nose, throat, and middle ear.

FOREIGN BODIES in the ear are not common or important except as furnishing to incompetent and rash attendants opportunity for improper and sometimes most injurious interference. This should be carefully avoided. Let alone, none but gunshot missiles or living insects can often occasion the slightest damage, except as forming nuclei for subsequent collections of cerumen.

It is the injury inflicted in efforts to remove them that is responsible for numerous untoward results, occasionally fatal. Rarely will any such object be thrust primarily beyond the cartilaginous portion of the canal, whence its extraction by any competent method should be easy. It is only after family or friend or incompetent medical man has pressed it deeper, and too often wounded or irritated to marked swelling the tissues about it, that the condition assumes any importance. Then the panic which assumes that it "will certainly go to the brain" must first be allayed; the patient quieted to bear examination, which previous abuse has taught him to dread, and the ground clearly taken that the intruding mass will be at once removed only if this can be safely done. To counsel delay *after* failure is apt to seem a reason for immediately seeking another and more vigorous attendant. Careful examination should first be made to determine the presence of the alleged foreign body, and this should begin with the other ear, not only that the configuration of the parts may be noted, but because in the excitement one ear may be receiving attention belonging to both or to the other alone. If there is, in fact, a body to be removed, the syringe and water of about 105° F. (40.5° C.) should be used as above directed, and, unless there has been very bad mishandling, there is likely to be little difficulty in washing out the intruder.

Should there be firm impaction in the bony canal or such swelling of the soft parts as to defy this procedure, it is best to use the water hotter still to reduce the inflammation and then to wait until the conditions are more favorable. Urgent symptoms may forbid this delay; then if vigorous syringing is unavailing, other instruments, such as a fine loop of wire or a blunt hook, may be tried in skillful hands, usually under general anesthesia, unless the patient is in perfect control. All but **specially adapted forceps** are commonly worse than useless and apt to force the body deeper. The **agglutination method** may suit those who fear to use water lest it swell some bodies and cause seeds to germinate before they can be removed; but hours can rarely be spent over such matters. If the body really needs removal it is safer to lay the soft parts forward by a free **incision** behind the auricle, and in the shorter and wider naked canal to use efficient leverage or bold chiseling to free and extract the mass. The injury thus surgically inflicted should be healed in a week; what will be done in blindly groping in the depths of the ear may never be repaired, and the life as well as the hearing may be sacrificed by such "conservatism."

If after syringing vainly an impacted seed it is decided to wait for reduced inflammation, a few drops of **carbolated glycerin** will serve as a sedative astringent and will dehydrate the seed as much as hours of syringing could swell it. So the science of those who syringe with substitutes for water is as wasted as that which floated up leaden shot with mercury instead of turning the ear down to let them fall out. **Gravity** can often be utilized in thus inclining the head, and **gentle rotary rubbing** in front of the ear will often coax out the foreign body. An **air-douche** with the Politzer bag or other means will sometimes best remove light substances, proving as efficacious as the old-fashioned, but reprehensible, "box on the ear" which has sent many a cherry-stone or pebble flying out across the room. The ear should be directed downward, drawn straight, and relieved of any pressure of the jaw-condyle by opening the mouth.

OTOMYCOSIS, or the growth of aspergillus or other molds in the auditory canal, is a rare affection, practically an eczematous inflammation with this infection as an accidental sequence and persisting irritant. Such organisms cannot flourish in a dry ear. It should be well cleansed and rigorously mopped with **hydrogen dioxide**, best that containing 60 per cent. alcohol, then dried with all thoroughness, and dusted with **boric acid.** Instillation of **borated alcohol** may precede this last, if it does not irritate too much. In the very rare instances when a few repetitions of this procedure fail of complete success, some of the many other commended drugs may be tried. As the growth may have penetrated deeply into the epithelium, no single treatment can be trusted to have destroyed every hypha and spore, and a non-mycotic eczema may remain to be cured, and here **silver nitrate** is often our best antiseptic and astringent.

HYPEROSTOSIS.—Exostosis and hyperostosis are generally self-limiting affections, very rarely in America calling for operation, but sometimes due to a hidden suppuration which they seriously complicate, and other new growths are too infrequent to call for special discussion.

B. Alexander Randall,
Philadelphia.

EXTRA-UTERINE PREGNANCY. See Pregnancy.

EYE AND APPENDAGES, INJURIES OF. See Cornea, Eyelids and Other Eye Structures.

EYELIDS, DISEASES OF THE.

—INFLAMMATION OF THE EYELIDS. (See BLEPHARITIS, volume i.)

INJURIES OF THE EYELIDS.

The lids may be the seat of all kinds of injuries, and, on account of the looseness of the skin over the overlying tissues, edema and ecchymosis are usually present.

Abscesses of the lid give rise to a localized red swelling, associated with more or less edema and hyperemia of the entire lid and the conjunctiva lining it. Throbbing pain in the eye and head and some fever accompany its formation. Abscess of the lid is usually the result of traumatism, but may be secondary to periostitis or caries of the margin of the orbit.

Treatment.—If there be a solution in the continuity of the lid, the edges of the *wound* should be carefully approximated with **sutures** and evaporating lotions, like dilute **lead water** and **laudanum,** should be applied. Simple *ecchymosis* of the lids, usually designated as "black eye," should be treated with **ice-compresses** and **lead water** and **laudanum.** When an *abscess* is present, **hot fomentations** are useful until fluctuation is detected. An **incision** should then be made into the abscess parallel to the muscle-fibers.

HORDEOLUM (STYE).—Hordeolum is a circumscribed purulent inflammation situated at the follicle of an eyelash. At first there is a hard swelling, with more or less involvement of the entire lid. A yellow head soon caps the little tumor, and, if allowed to go on, this will break open and the contents be discharged. There is usually a feeling of great tension in the lid until the abscess is opened, and there may be slight febrile disturbance.

Hordeolum is found chiefly in the young, especially in anemic girls, where it is the expression of a constitutional disturbance. Habitual constipation has been assigned as a common source of the inflammation. When associated with boils, etc., the urine should be tested for sugar, especially in adults. Uncorrected ametropia is a frequent cause.

Treatment.—The inflammation may at times be aborted in the earliest stages by **hot boric lotion,** by **massage** with **yellow oxide** of **mercury,** by applications of **silver nitrate,** or by painting the swelling with **collodion.** If this fails, suppuration should be encouraged by **hot applications,** and a free **incision** be made as soon as pus is suspected. **Sulphide of calcium** internally is frequently of service. The opsonic index of the blood against staphylococci may be taken. It will often be found abnormally low; in these cases **staphylococcic vaccines** should be tried.

> **Suction hyperemia** for styes and furuncles of the lids may be applied by means of a rubber ball and glass cups. The cup is as small as will include all the diseased area. The negative pressure is that made by a round ball two inches in diameter, or 30 mm. of mercury. The cup is left in position not more than one-half hour. If this pressure or time is exceeded, there may be hemorrhages. The results were prompt and favorable. Hoppe (Münch. med. Woch., Nu. 40, 1906).
>
> The writer has found the most satisfactory treatment to be the following. With a small pair of forceps pull out each hair which shows a collection of pus, or even a red spot, at its root. Direct the patient to apply, from ten to thirty times a day, a

collyrium prepared as described later. If examined again in a few days, the inflammation as the rule will have ceased; but if any pustule is then seen, immediately pull out the eyelash, and continue the applications as before. Ordinarily, everything will have been finished in three or four weeks, and new hairs will rapidly take the place of those epilated. The remedy used is a combination of astringents, known formerly as *lapis divinus.* The formula, given by Sabouraud, is:—

℞ *Potassium nitrate,*
Copper sulphate,
Alum, ...āā 100 Gm. (3⅓ ounces).
Camphor ... 5 Gm. (1¼ drams).
M. Form into pencils.

A solution of this may be made with rose water of the strength of ½ per cent, Sabouraud (La Clinique, June 14, 1907).

During the acute stages **hot applications** are advised. As soon as the acute stage has somewhat subsided, the writer applies locally the following mixture:—

℞ *Tincturæ arnicæ*..... 16 Gm. (℥ss).
Tincturæ opii,
Liquoris plumbi subacetatis dil, ...āā 8 Gm. (ʒij).
Aquæ destillatæ, q. s.
ad .... 90 Gm. (℥iij).
M. Sig.: Apply locally by means of absorbent cotton at bedtime.

After the disappearance of the stye for a period of four weeks, the following antiseptic ointment is employed:—

℞ *Hydrargyri chloridi corrosivi* ...... 0.008 Gm. (gr. ⅛).
Petrolati albi 8.0 Gm. (ʒij).
M. Sig.: Externally.

This should not be merely smeared over the lids, but be applied with gentle massage every night. Prior to the application of this antiseptic ointment hot compresses should be applied to stimulate the circulation of of the margin of the lids. Brav (N. Y. Med. Jour., Sept. 18, 1909).

CHALAZION.—Chalazion is a hard swelling which forms in the lids in connection with a Meibomian gland. It varies in size from the head of a pin to a large pea. Suppuration may occur, and the viscid contents of the tumor be discharged on the conjunctival surface of the lid, or the growth may be wholly absorbed and disappear. As a rule, it causes but little pain; rarely at times, however, it takes an acute form, when the symptoms resemble those of hordeolum. Chalazion originates in a chronic inflammatory process in the connective tissue surrounding a Meibomian gland, especially where there is uncorrected ametropia. It usually occurs in adults.

Treatment may be either abortive or radical. The former is rarely successful, but **massage** of the growth may be tried, using an ointment of **yellow oxide of mercury** or **iodide of cadmium.**

The radical plan consists in the **removal** of the growth **by operation,** either from the skin or conjunctival surfaces. If the tumor shows evidence of having broken down, it had better be removed from the latter surface. This is accomplished by means of a vertical incision into the growth with a sharp scalpel, after thorough cocainization of the conjunctiva, and the removal of the contents of the sac with a small curette or scoop especially constructed for this purpose. If, on the other hand, the growth be large and firm, and gives no evidence of having undergone degeneration, it is better to remove it from the skin-surface by means of a formal dissection. For this purpose it is customary to control the hemorrhage by means of a clamp which includes the field of operation in its area, and to insert several stitches after the tumor has been excised. Care should be taken that all of the growth be removed to prevent recurrence.

> The writer has found that a **marginal incision** is especially useful in the treatment of chalazia of the upper lids which are situated near the margin, and of most of those in the lower. The only cysts which are unsuitable for this operation are those which are found in the highest parts of the upper lid. The incision is made with a small double-edged knife, either in the intramarginal line or in the thickness of the tarsal plate itself, and the deeper parts enlarged by a movement of the blade from side to side without enlarging the opening. The contents of the tumor are then expressed by the fingers or evacuated by the scoop, if required. Antonelli (La Clinique Ophtal., July 10, 1905).

CUTANEOUS DISORDERS OF THE EYELIDS.

ECZEMA.—Eczema is one of the most frequent of palpebral affections; it is usually met with in children in its moist form (crusta lactea). It is generally secondary to phlyctenular conjunctivitis, and results from the continued irritation of the lids by the profuse lachrymation incident upon this form of conjunctivitis. A similar eruption is seen in adults, especially in the lower lid, when the lachrymation is secondary to lachrymal disease or catarrh of the conjunctiva.

Treatment.—Removal of the scabs with a warm solution of **bicarbonate of potassium** without provoking any bleeding is advisable. After the lids have been thoroughly dried, a solution of **silver nitrate,** 20 grains (1.3 Gm.) to the ounce (30 Gm), should be carefully applied to the raw surfaces. The lid should then be covered with an **oxide of zinc** ointment. Either the plain ointment may be employed or one consisting of equal parts of oxide of zinc and vaselin to which 20 grains (1.3 Gm.) of **calomel** have been added. A mixture of **tragacanth,** 5; **glycerin,** 2; aquæ dest., ad 100, is of service in the treatment of fissures on the angles of the lids in scaly and moist ezcemas of the latter.

HERPES ZOSTER OPHTHALMICUS is an inflammatory affection of the skin, characterized by the formation of vesicles along the terminal expansions of the supraorbital division of the fifth nerve, and sometimes its nasal branch, and more rarely the infraorbital division of the same nerve as well. The vesicles are generally grouped together and have an inflamed base. At first they contain a limpid fluid, but this soon becomes clouded; the vesicles then dry up and form scabs, which fall off and leave deeply pitted scars that persist during the remainder of life. As a rule, the appearance of the vesicles is preceded by severe neuralgic pain in the course of the affected nerve-branches, and there is some fever. The pain generally subsides with the efflorescence of the vesicles. The eyeball is sometimes implicated, either in the form of a keratitis, iritis, or iridocyclitis. Although the intraocular tension is not infrequently somewhat diminished in the early stage, I have noted the occurrence of the disease with acute glaucoma.

It usually occurs in the old and feeble, although it has been seen in young and healthy individuals.

Treatment is wholly symptomatic, and consists in sedative local applications of **lead water** and **laudanum,** or in dusting **rice starch** over the affected areas. **Morphine** should be administered internally for the relief of pain, and tonics should be directed toward building up the system. For the severe neuralgia which frequently remains after the subsidence of the inflammation, **croton-chloral hydrate**, in doses from 5 to 10 grains (0.3 to 0.6 Gm.) every four hours, and the use of a mild **galvanic current** have been highly recommended. Any ocular involvement must be combated by the proper remedies. The affected eye should be protected by a bandage.

TUMORS OF THE EYELIDS.

CARCINOMA of the eyelids takes the form of *rodent* or *Jacob's ulcer*, occurring in adults, and characterized by a slowly progressive, but destructive, ulcerative process, by which the lids and the neighboring tissues are gradually consumed. The first appearance is that of a pimple, usually at the inner canthus, which becomes indurated and covered by a scab.

Treatment should consist in the early and complete removal of all the diseased tissue by **dissection**, followed in some cases by the application of **chloride of zinc** or even of the **actual cautery.** Considerable improvement and even cure have followed the use of **radium,** and this plan of treatment may be essayed for a time in cases where the rodent ulcer has destroyed much tissue.

XANTHELASMA.—Xanthelasma are yellowish or buff-colored *plaques,* which are occasionally found upon the eyelids. These patches are slightly raised above the surrounding skin, and are frequently semicircular in shape. They are often symmetrical, and have a predilection for the inner part of the upper lids. They are more common in women than in men, and occur in adult life as a result of hypertrophy of the sebaceous glands, with subsequent fatty degeneration of the subcutaneous connective tissue.

Treatment.—As these growths have no significance other than a cosmetic one, they should not be interfered with, save when they are large and disfiguring, in which event they may be removed by careful **dissection**, or by **electrolysis.**

Palpebral tumors may also be made to disappear by repeated applications of a solution of **monochloracetic acid.**

MOLLUSCUM CONTAGIOSUM.—This consists in a white tumor, varying in size from the head of a pin to that of a pea, that forms in the skin of the lid. The disease begins in a sebaceous gland, and is found chiefly among badly nourished children.

Treatment.—Treatment consists in **incision** and touching the interior of the growth with solid **nitrate of silver** stick after squeezing out its contents.

PAPILLOMATA, SARCOMATA, AND EPITHELIOMATA are all found on the lids, but, as they have no characteristics different from those which they possess elsewhere, do not require detailed study.

> Case in which a man, 55 years of age, presented a triangular ulcerated area that involved the outer part of the skin of the lower lid. Epithelioma was diagnosticated. The surface was cleansed and powdered **potassium chlorate** was rubbed into the floor and edges of the ulcer at first every day, later every other day. After a week of this treatment the ulcer gradually diminished and finally healed. Zentmayer (Ophthalmic Record, Aug., 1907).

Remarkable case in which a large epithelioma beginning at the margin of the lower lid and extending across the entire cornea completely concealing it with, of course, total blindness of the eye. Immediately upon striking his head accidentally against a tree the affected eye received a violent contusion with profuse hemorrhage. When this was arrested the man found that he had recovered his sight. The cornea was found entirely uncovered and intact and the remains of the tumor formed a thick fringe about the lower border on the nasal side. Instead of forming an integral part of the cornea the tumor was evidently simply superimposed upon that membrane, which retained its transparency intact.

A few similar cases have been previously reported. It may therefore be advisable, in tumor of the anterior segment of the eyeball, to make a careful dissection to determine the condition of the subjacent cornea. Dujardin (Clin. Ophtal., No. 8, p. 119, 1908).

HEMANGIOMATA, OR NEVI, occur on the lids in two forms: telangiectasis and cavernous hemangioma. The former are composed of dilated capillaries and take the form of small, bright-red or port-wine colored spots; the latter consists of dilated and anastomosing venous spaces in the subcutaneous tissue. They appear as small, bluish tumors, and increase in size on crying and lowering the head.

Treatment.—Both forms may be removed by **electrolysis** or by application of **carbonic acid snow.**

SYPHILIS OF THE EYELIDS.

Primary sores are found on the margin of the lids, usually at the canthi. The first appearance is that of a pimple, which gradually breaks down into a depressed ulcer, with a characteristic induration of the base. The glands in front of the ear and at the angle of the jaw are almost always involved, and the usual constitutional signs of syphilis follow. The contagion is carried to the eye, as a rule, by the finger; though in some instances it has followed a kiss or the filthy custom, practised in some communities, of attempting to dislodge foreign bodies from the eye by the tongue.

Rarer forms which occur in the secondary and tertiary stage of the disease consist in a marked induration and swelling of the entire lid, followed by ulceration of the margins of the lids and the loss of the cilia. Syphilis of the lids must be diagnosed from suppurating styes and chalazia, from lupus vulgaris, and from chronic cases of dacryocystitis.

Treatment.—Chancres should be dusted with finely powdered **iodide of mercury,** or application made to them by the **black** or **yellow wash.** General **mercurial treatment** or **salvarsan** should be employed as soon as the diagnosis of syphilis is assured.

NEUROSES OF THE EYELIDS.

BLEPHAROSPASM is an involuntary contraction of the orbicularis palpebrarum, and may be either the result of irritation of the ophthalmic division of the fifth nerve by reflex action, as in disease of the cornea, etc., or it may be an essential spasm, occurring in eyes that are perfectly normal. A slight twitching in a few fibers of the muscle is not unusual in ametropia and may be made to disappear by the adjustment of the proper glasses.

Treatment should aim at the cause. In severe cases hypodermic injections of **morphine** into the lids may be necessary, or even **subcutaneous division of the nerve.**

The writers have successfully practised **section of the facial nerve,** followed by immediate anastomosis with the eleventh pair in a severe case of this affection, which had been rebellious to both medical and surgical attempts at cure. Section of the facial nerve is followed by a temporary paralysis; the latter soon disappear. Abadie and Cunes (Arch. d'oph., April, 1905).

Injections of 80 per cent. alcohol combined with **cocaine** or **stovaine** are a safe, simple, and effective means of treatment of obstinate facial spasm. The treatment is applicable both in simple spasm and in the complicated facial tic douloureux. The injections should be made at the point of emergence of the facial nerve. The paralysis which follows the injections should cause no anxiety, no matter how long it lasts, so long as there is no tendency to alteration of the cornea and the eyes close sufficiently during sleep. Valude (Tribune méd., vol. xli, p. 232, 1908).

The writer makes subcutaneous injections of **alcohol** superficially in the neighborhood of the stylomastoid foramen under the skin, in the region of the supraorbital nerve and of its palpebral filaments, and in the distribution of the orbital filaments of the facial so as to affect the orbicularis; 30 parts of absolute alcohol and 60 of sterilized water constitute the injection employed without an anesthetic. A syringeful (Pravaz) is used for the supraorbital region, and in inveterate cases of essential blepharospasm a similar quantity is employed for the infraorbital region. A single injection under the skin of the lid, in the center and parallel to the free border, suffices in spasmodic entropion (children and the aged). Several injections may be made daily or at longer intervals until cure or considerable amelioration is obtained. Fumagalli (Annali di Oftal., vol. xxviii, fasc. 3, p. 162, 1909).

PTOSIS is a drooping of the upper lid over the eyeball, with inability to raise the same. When not congenital, or the result of thickening of the lid from inflammation, it is due to paralysis of that branch of the third nerve which supplies the levator palpebræ superior. Ptosis is frequently associated with palsies of other muscles supplied by the third nerve, and when it is an isolated symptom suggests central disease.

Treatment.—If of recent origin, alteratives, such as **mercury** and **potassium iodides**, should be administered in high doses; if of long standing, recourse must be had to operative procedure. That of **Panas** is preferred. This **operation** has for its object the securing of a connection between the lid and the frontalis muscle by means of a skin-flap. This flap is obtained by inserting a horn spatula under the upper lid, and by making a horizontal incision about 5 mm. above the margin of the lid through the skin and subcutaneous tissue; another incision, parallel to this and about 1 mm. long, is made through the eyebrow, and is extended as far as the periosteum. Two incisions are then made at right angles to the first inferiorly, the flap of the skin remaining between the two primary incisions is undermined, and the tongue of skin drawn up under the bridge and held in position there by sutures.

A somewhat recent **procedure** introduced by **Motais** is coming into favor, and consists essentially in making the superior rectus muscle available for replacing the levator.

> The writer speaks favorably of **Motais's operation**, which consists in the transplantation of the middle portion of the insertion of the superior rectus to the upper margin of the tarsal cartilage. He has performed it on five patients. In the majority the effect was insufficient; so in two the operation was supplemented by

the excision of a strip of tissue, 3 to 4 mm. wide, involving the entire breadth and thickness of the lid. In all a slight degree of lagophthalmos was produced, requiring a strong innervation of the orbicularis to close the lids. Otherwise the cosmetic and optic effect was excellent. A. Elschnig (Med. Klinik, May 15, 1910).

LAGOPHTHALMOS.—By this term is meant an inability to close the eyelids. It is either due to paralysis of the facial nerve or is the result of some condition within the orbit, or in the eyeball itself, which causes the globe to protrude between the lids. As a result of the exposure to which the cornea is subjected, it frequently ulcerates, and, unless proper procedures be inaugurated, the eye is lost.

Treatment.—If due to paralysis of the seventh nerve, the cornea should be protected by carefully **bandaging** the eye during sleep, and by cleansing the conjunctival *cul-de-sac* with frequent washings of **boric acid solution.** The primary cause of the paralysis must be treated, and **galvanism** and hypodermic injections of **strychnine** may be tried. If the degree of lagophthalmos be excessive, the bandage should be worn constantly, and at times **tarsorrhaphy** is necessitated. This operation consists in uniting the the margins of the lids by means of sutures after their skin has been removed from the ciliary border by a sharp knife.

CONGENITAL ANOMALIES OF THE EYELIDS.

Absence of a part of or all of an eyelid or of both eyelids has been noted, though very rarely. *Cleft eyelid,* or *coloboma* of the lid, has also been observed—usually in the upper lid. At times this deformity occurs on both sides.

Case of congenital coloboma of the left upper lid met with in a child 2½ years old. The defect was triangular with its base at the ciliary margin, its apex about the middle of the lid. The margins of the coloboma were not provided with lashes. The fissure was closed by means of a **plastic operation.** The writer says that only 80 or 90 similar cases have been reported. Meyer (Berl. klin. Woch., May 20, 1907).

EPICANTHUS.—This applies to the development of a broad fold of skin which extends from the inner border of the eyebrow to the side of the nose, its outer border being concave. This anomaly is usually associated with ptosis, or drooping of the upper lid over the globe.

ACQUIRED ANOMALIES OF THE EYELIDS.

It sometimes happens after injury, and especially after burns, that the edges of the lids become united to each other. This condition is known as *ankyloblepharon.* If the adhesion occurs at the outer angle of the lids, *blepharophimosis* is said to be present.

SYMBLEPHARON is a union between the lid and the eyeball, and is generally the result of a burn or some severe inflammation of the conjunctiva which has produced great shrinkage of the conjunctiva and cicatricial change in the lids. The band of union may be but a delicate process of connective tissue, or the lid may be held down to the globe by an extensive cicatrix.

Treatment.—If the band be but slight, it may be severed by **ligature**; but if the attachment be more extensive, transplantation of healthy skin into the *cul-de-sac* may be necessary (**Teale's operation**), or the procedure of Harlan may be adopted. This author frees the lid from the globe by careful dissection of the band of attachment, and then makes an incision through the whole thickness of the lid along the margin of the orbit. A thin flap is then obtained from the skin below the lid, which is turned upward, as on a hinge, so that its raw surface is brought into contact with the inner surface of the lid, while its smooth surface presents toward the globe.

> The advantage of **paraffin plate** for holding mucous or Thiersch **grafts** in place in the fornix of the eyelids is obvious. It can do no harm to the cornea, and it can be built up as required to fit any conjunctiva *cul-de-sac* that has to be lined with a Thiersch graft. The graft will adhere to the paraffin, so that it can be evenly smoothed out on it, and thus perfect coaptation is secured between the graft and the raw surface of the *cul-de-sac*. To accomplish this, the graft should be thin and large enough to cover all raw surface, no suture being required. With perfect coaptation the graft will have secured a firm hold at the end of forty-eight hours and the plate can be removed for cleansing the eye. In case of restoration of the socket for prothesis, it may be left in place for a considerable time, for the sac can be cleaned by irrigation through the holes in the plate. If it is so large that there is difficulty in removing it, it can be cut in two and the subsequent treatment continued with a plate that can be more easily inserted. The paraffin should be hard, with a melting point not lower than 150° F. (65.6° C.). The Thiersch graft should be thin and cut from the least hairy part of the arm or leg, and it is to be transferred to the paraffin plate directly from the razor. The plate is thus covered with the graft; the raw side outward is inserted into the new fornix. The author has thus operated upon 8 severe cases of symblepharon with good results. Wilder (Jour. Amer. Med. Assoc., Aug. 25, 1906).

Blepharophimosis may be corrected by dividing the outer canthus by a sharp pair of scissors, or by uniting the conjunctiva and the skin-surface by sutures.

ECTROPION. — Ectropion, eversion of the eyelid, may be caused by traumatisms, especially burns, the cicatricial contractions drawing its tissues outwardly. Muscular or senile ectropion is seen in the aged, as a consequence of atrophy of the palpebral portion of the orbicularis and relaxation of the tissues.

Treatment.—In senile ectropion the deformity may usually be overcome by means of **Snellen's sutures.** This consists in burying a suture, which is entered at two points, one-third of an inch distant from each other, in the mucous surface of the lid, and passing deeply into the tissues between the skin and the mucous membrane. It is brought out upon the cheek, where the ends are tied over a piece of drainage-tube.

In cicatricial ectropion it is necessary to include in the **incision** the scar-tissue which has occasioned the eversion of the lid. If the cicatrix is small, **Wharton Jones's operation** will suffice. This consists in excising the cicatrix by means of a V-shaped incision. After the edges of the incision have been freely loosened from the sublying tissue they are approximated so as to form a Y. If the cicatrix be extensive, or if there has been much destruction of the skin of the lids and the neighboring tissues, **transplantation of skin** from neighboring or distant parts is necessary.

> The writer recommends and describes a method which he has employed for many years with success in entropion and ectropion and some other conditions of the lids. It requires but two instruments which are

figured, a short **galvanocautery** point **and a lid clamp.** He usually employs local anesthesia with 4 per cent. cocaine on the conjunctival surface, but in nervous, sensitive patients it is necessary to employ nitrous oxide, bromide of ethyl, chloroform, or ether. If ether is used it must be removed before the approach of the hot cautery point. The lid clamp is adjusted with its straight bar 6 mm. from the lid margin. The galvanocautery point is applied to the surface with considerable pressure. The button on the handle is pressed down to turn on the current, while the point is quickly pushed through the cartilage and as quickly withdrawn. The punctures are made 4 mm. from the lid margin and separated from each other by an interval of 4 mm. These should be made on the side on which we wish the contraction to take place, namely, the conjunctival surface in ectropion and the skin surface in entropion. If necessary we can repeat in a few weeks. From one to three sittings will accomplish as much as would a plastic operation. He has seldom seen any reaction follow, but if there is a little cellulitis and puffing of the lid, the use of continuous ice-pads for a day or two will control it. Two or three repetitions are generally required, at intervals of from two to four weeks, according to the case. The procedure is perfectly under control. In repeating the operation it is well to alternate the punctures, locating the second series between the first. The eschar of the cautery causes no disturbance and usually clears off in about a week. Fourteen cases are briefly reported, showing the effects of the procedure in the class of cases for which it is adapted. S. L. Ziegler (Jour. Amer. Med. Assoc., July 17, 1909).

A new principle in the treatment of ectropion. It consists in **shortening** the **tarsus** at the temporal extremity and then attaching this extremity to the periosteum of the temporal border of the orbit on a level, slightly above the lid commissure, if the lower lid is affected, and below the commissure if the upper lid is in fault. It is used for atonic ectropion, but the principle applies also in many cases of cicatricial ectropion, and it was in one of these patients, who had undergone six operations without success, that the writer did his first operation. The result was most satisfactory and has remained so for fifteen months. In some cases of atonic ectropion in which the author has tried the operation in its simplest form, removing a small piece of tarsus and anchoring the outer extremity of the periosteum, removing no skin and only a few cilia, the result has been satisfactory in every case. A. E. Davis (Jour. Amer. Med. Assoc., Nov. 18, 1911).

ENTROPION.—Inversion of the eyelid, the margin, its lids being rolled inward, may be *spasmodic,*—*i.e.,* due to overaction of the orbicularis through irritation from concomitant disorders, conjunctivitis, keratitis, etc., or to undue application of bandages after operation,—and *organic,* due to injuries, burns, ulcers.

Treatment.—The *spasmodic form* may readily be corrected by **excising** a narrow **strip of skin** from the lid parallel with its ciliary border. In *organic* entropion, on the other hand, it is necessary to **include the tarsus** in the operation, as this is usually distorted by the previous inflammation.

One of the best **procedures** for the cure of this deformity is that of **Hotz.** This is performed as follows: A transverse incision from canthus to canthus is made through skin and subjacent tissues, but, instead of being made near and parallel with the free border (as in the former methods), the incision is to follow the upper border of the tarsus. It therefore describes a slight curve beginning and ending at a point about 2 mm. above the canthus, but being 6 to 8 mm. distant from the free border in the center of the lid. While an assistant is holding the edges of the wound well separated, the surgeon lifts up with forceps and excises with scissors a narrow bundle of the muscular fibers which run transversely along the upper border of the tarsus. The sutures, which are to include nothing but the cutaneous wound borders and the upper border of the tarsus, are then inserted. The first suture is placed in the center of the lid; the curved needle, armed with fine, black, aseptic silk, is passed through the lower wound border; there taken again in the needle-holder, it is boldly thrust through the upper border of the tarsus and returned through the tarso-orbital fascia just above this border, and finally it is carried through the upper wound border. One similar suture is placed at each side of the central one, and these three stitches are usually sufficient to draw the skin of the eyelid up toward the upper border of the tarsus and establish a firm union between these parts. This artificial union produces a slight tension of the tarsal skin, which, however, is sufficient to relieve any ordinary degree of entropion. But when the lids have been badly contracted—when the palpebral aperture has become unnaturally narrow or the free border of the lid has become entirely merged into the plane of the conjunctiva—these complicated cases require, in addition to the above operation, such surgical measures as **canthotomy**, the restoration of the free border either by **grooving the tarsus** or by **grafting.**

DISTICHIASIS AND TRICHIASIS.

While distichiasis refers to the growth of the cilia along the outer marginal portion of the eyelid, trichiasis means a misplacement of the eyelashes. Both conditions are usually associated with entropion, especially when this condition is the result of chronic inflammation of the border of the lids.

Treatment. — **Epilation** or **removal of the cilia** by forceps may be tried if the stray cilia be not too numerous. **Electrolysis** may also be used in similar cases. Usually, however, **excision** of the **misplaced cilia** with the corresponding portion of the margin of the lid is necessary. This may be accomplished by making a V-shaped incision into the lid and by excising the flap so obtained, along with the truant cilia.

If the deformity be extensive, transplantation of the row of cilia is usually effected, and this is best accomplished by the **Jaesche-Arlt operation.** After a Knapp or a Snellen clamp has been applied to stop bleeding the lid is split in its whole length by a sharp knife; a second incision is then made through the skin of the lid about 5 mm. from its free margin and running its entire length. A semilunar flap of skin is then removed from the lid by carrying a third incision in a curve the entire length of the second incision. The edges of this incision are approximated by sutures, and the cilia drawn upward away from the globe.

William Campbell Posey,
Philadelphia.

F

FARCY. See Glanders.

FAVUS. See Hair, Diseases of.

FEBRICULA. See Miliary Fever.

FELON. See Tendons, Bursæ and Fasciæ, Diseases of.

FIBROID PHTHISIS. See Tuberculosis, Chronic Pulmonary.

FIBROLYSIN. See Hyoscyamine.

FILARIASIS. See Parasites, Diseases Due to.

FLAXSEED. See Linum.

FOOT-AND-MOUTH DISEASE. See Mouth, Diseases of.

FORMIC ALDEHYDE, or Formaldehyde.—This gaseous compound, discovered by von Hoffman in 1867, is produced when a current of air charged with vapor of methyl alcohol (wood alcohol, or refined wood spirit) is directed upon an incandescent spiral of platinum wire, or spongy platinum. By means of a suitable condensing apparatus a liquid called *formol* may be obtained, which consists of a solution of formic aldehyde gas in methyl alcohol.

A watery solution of the gas is the *formalin* of commerce, which contains 40 per cent. of formaldehyde.

Formic aldehyde is also known as methyl aldehyde and oxymethylene.

When formic aldehyde is heated or strongly concentrated, it is converted into a white crystalline powder (*paraform*), which possesses most of the characteristics of formic aldehyde, owing to its gradual reversion to the gaseous state.

When *paraform* is volatilized it reverts to the gaseous form, but is redeposited as a sublimate in the crystalline form. Surgical dressings and bandages are impregnated with formic aldehyde in this way. The term "formalhyde" is commonly used instead of the more correct term "formic aldehyde."

PREPARATIONS.—When *formalin* (the 40 per cent. solution of formaldehyde gas) is heated in a dish or vessel, formaldehyde is disengaged and, at the same time, paraform crystals are deposited on the interior of the vessels. *Paraform,* or the polymerized form of formaldehyde, is also known as paraformaldehyde, paraformic aldehyde, triformol, trioxymethylene, and dry formalin, and may be obtained in the form of white, crystalline powder, or molded into pastils.

Liquor Formaldehyde, U. S. P., is an aqueous solution of formaldehyde which contains 37 per cent. of the gas. It occurs as a clear liquid which is pungent and irritating to the mucous membranes. It mixes readily with water and alcohol in any proportion, but the solution becomes milky on standing owing to the separation of the formaldehyde from its excipient. It should be kept in the dark and in a cool place.

Various convenient preparations of these various agents are available in the shops in the form of pastils, candles, etc., which greatly simplify their use.

PHYSIOLOGICAL ACTION.—Formaldehyde has an intensely irritating effect on the mucous membrane of the eyes and air-passages. When injected subcutaneously in dogs, Pilliet observed congestion and degeneration change in the kidneys, liver, and spleen.

According to Benedicenti formaldehyde is a blood-poison. Introduced into the body, it causes excitement followed by slow asphyxia, and added to the blood outside the body it destroys the corpuscles and liberates hematin. The last body is formed without any preliminary change of oxyhemoglobin to reduce hemoglobin.

Formaldehyde is not eliminated as such from the organism, but probably undergoes oxidation in the tissues. Polacci's reagent gives, as the writer found, the same reaction with mucin and mucinogen as with formaldehyde, and this was the source of error in the previous investigations. Gianelli (Riforma Medica, Nov. 18, 1903).

Formaldehyde appears in the urine in only 52 per cent. of patients taking urotropin. The reaction of the urine is of no importance. Alkalies, taken with or in combination with urotropin, have no effect on excretion. The duration of the excretion of formaldehyde is about from four to six hours. An increase of dose does not affect excretion in negative urines. Urotropin is practically symptomless in an average dose. The urine of all patients taking urotropin should be tested for formaldehyde. Patients not excreting formaldehyde are symptomless, regardless of the amount of urotropin taken. L'Espérance (Boston Med. and Surg. Jour., Oct. 24, 1912).

The writer gives the results of experiments made with *Burnam's test* for formaldehyde in the urine. His interest in the subject was aroused by the article of L'Espérance on the results of the reaction as tested in the Massachusetts Hospital. His own results are different in many respects from those of L'Espérance. Burnam's test consists in a color reaction in the urine of persons who have taken hexamethylenamine. The technique is given by L'Espérance as follows: "To about 10 c.c. of suspected urine in a test-tube at body temperature is added: (1) of solution phenylhydrazin and hydrochloric acid (0.5 per cent.), 3 drops; (2) of solution sodium nitroprusside (5 per cent.), 3 drops; (3) of saturated solution sodium hydrate, a few drops poured along the side of the test-tube. As this latter solution diffuses throughout the urine in the tube, if formaldehyde is present (or the urine is positive), a deep purplish-black color is seen, quickly changing to dark green, gradually getting of a lighter shade of the same color, and finally pale yellow." When there is no formaldehyde in the urine a reddish color appears, changing to light yellow. The average time of appearance of the drug in the urine is about one hour after ingestion. It continues from four to six hours with its maximum at two hours. Jenness followed the same technique on two groups of men, 100 each. The first group were given 10 grains at 6 P.M. and a second dose at 6.30 the following morning, and the urines were examined at the end of five hours. The second group received 20 grains at 6.30 A.M. and the urines were examined at the end of two hours. The reaction in every case took place immedately, but varied slightly from those of L'Espérance. The deep purplish black is not constant. In many the color was not a deep purplish black, but purple changing to a green (not dark green), and finally to a pale yellow. A rather constant diagnostic point in the positive urines was the striking rapidity of the color formation and a peculiar method of diffusion through the upper strata of the fluid, going down in jets, as it were, from the top and diffusing in the lower strata. In the negative urines the test agreed in the main with those of L'Espérance, except that the end reaction was a greenish yellow. In the first group of 100, 42 per cent. of the urines were positive and 53 per cent. were positive in the second group, the total percentage in the 200 together being 47.5, or 5 per cent. less than that reported by

L'Espérance. B. F. Jennes (Jour. Amer. Med. Assoc., March 1, 1913).

POISONING BY FORMIC ALDEHYDE. — Concentrated aqueous solutions in contact with the skin are somewhat like carbolic acid. The skin becomes rough and whitish; a sharp stinging is felt if the skin is abraded.

Formaldehyde is a potent poison when the solution is strong or the quality ingested large, differing but little in the degree of intoxication it produces from that of carbolic acid, that is to say, phenol. A number of fatal cases have been recorded, in which the main symptoms were: A pricking or burning sensation in the pharynx and esophagus. Severe epigastric pain, which radiates in various directions, repeated vomiting of blood-stained mucus, vertigo, dyspnea, a weak and rapid pulse, unconsciousness — sometimes prolonged and suggesting cerebral apoplexy — lapsing into coma. The symptoms may come on at once if the poison is ingested while the stomach is empty; or they may be delayed, in so far as the general phenomena are concerned, if the stomach contains food. A large dose may produce death in a few moments.

> Case of poisoning due to swallowing a quantity, about 1 ounce (30 c.c.), of formalin. There was vertigo, unconsciousness, and implication of the respiratory rather than the circulatory system. The predominance of cerebral symptoms, leading to early death, gave little opportunity for the development of signs of irritation of the kidneys and the alimentary canal, apart from the intense pain in the latter and the initial vomiting. Watt (Brit. Med. Jour., Aug. 17, 1912).

The intravenous injection of weak formaldehyde solution has been tried in the severe puerperal sepsis, but the margin of safety was found to be so slight that the method was abandoned.

Treatment of Formaldehyde Poisoning.—The most efficient agent to oppose the toxic action of formaldehyde is the official solution of **acetate of ammonium**, the **spirit of Mindererus**, with **copious draughts of water**. **Ammonia water** well **diluted**, the **aromatic spirit of ammonia**, or one of the **salts of ammonium**, especially the above mentioned, also in free dilution are antidotes. **Lavages** of the **stomach**, followed by the use of demulcents, **olive oil**, **starch water**, etc., are also regarded as antidotes. **Morphine** should be given hypodermically to relieve the suffering which is usually very intense.

> Large doses of **lime water**, a pint being given repeatedly, in a marked case of formaldehyde poisoning. Shortly after taking the first dose the patient was able to speak and complained of very severe burning in his mouth and stomach. The author ordered more lime water, each time giving him a full pint until he had taken four pints. The watery and salivary discharges ceased, and the burning sensations grew less marked. About fifteen minutes later the patient was able to walk and said he only had a little pain in his stomach. He did not get any other treatment, made a perfect recovery, and, at the same time, was perfectly sobered up. Stephen Fisher (Medical Council, July, 1904).

USES IN DISINFECTION. — The chief use of formaldehyde so far has been as an antiseptic and disinfectant. It permeates everywhere, while being cheap and easily handled and less dangerous than corrosive sublimate.

In disinfecting a room the doors,

windows, etc., must be made perfectly tight, as the diffusive power of the gas is very high. The gas, which is very irritating to the eyes and respiratory tract, may be generated outside the room in one of the various generators to be had, and the gas conducted by a tube through the keyhole. Some forms of apparatuses are operated within the apartment. The pastils, candles, etc., available in the shops are thus used. After a sufficient amount of gas has been set free in the apartment, it is left for twenty-four hours. Length of exposure appears to be secondary to the quantity of gas used. An excess is recommended by most authorities.

Superficial instruments, bedpans, urinals, bedding, surgical dressings may be sterilized in small closets or in suitable receptacles. Formaldehyde does not seem to affect the coloring matter of the wall-paper, drapery, or garments (except light shades of violet and light red), and for this reason it is preferable to chlorine as a disinfectant.

If the fabrics or utensils can be moistened the action of the gas is rendered more active. A 1 per cent. solution suffices for all purposes. After the disinfection is completed the rooms should be aired for some hours, to rid it of all gas, owing to its irritating action on the throat and eyes. If the room must be promptly reoccupied, as in hospitals, hotels, barracks, etc., a 20 per cent. solution of ammonia sprayed into the room, by neutralizing the formaldehyde, rids the air of its pungency.

Attention called to the power of this gas to penetrate the cell walls of bacteria and destroy them. It retards their growth and destroys invading germs when they attack the respiratory tract. It can only be depended on to destroy pathogenic germs whose structure permits sufficient penetration to alter their protoplasm, and for this purpose it has no equal as a disinfectant. W. K. Jaques (Merck's Archives, Mar., 1900).

Formalin (a 40 per cent. aqueous solution of formaldehyde) for disinfecting purposes after contagious disease is a cheap and certain destroyer of noxious germs. Basil Kluczenko (Wiener klin. Woch., Oct. 11, 1900).

Of disinfectants that are efficacious, innocuous, automatic, and inexpensive, the best is formic aldehyde. It forms an odorless compound with ammonia, which becomes useful, after disinfection, for removing the smell. It also makes gelatin insoluble, forming a hard, transparent mass. It is antiseptic, diffusible, and penetrating. Alfred Martinet (Presse méd., April 30, 1902).

The procedure recommended by the Maine State Board of Health for the disinfection of rooms after their use by patients suffering from contagious disease is as follows: Potassium permanganate and formaldehyde are mixed together in the proportion of 6½ ounces of the former to each pint of the latter, and placed in a vessel of considerable size. The room is then closed for four hours, when disinfection is said to be complete. Two pints of the formaldehyde are to be allowed to every 1000 cubic feet of space. Both on the score of simplicity and cost the method has much to recommend it. (Treatment, Dec., 1905).

While urologists have used formaldehyde for the sterilization of sounds and cystoscopes, surgeons, obstetricians, and general practitioners have failed to avail themselves of its valuable properties. The experimental researches and clinical experience of the writer showed it to be in many respects superior to the methods of sterilization now in vogue. All porous materials placed in a formaldehyde vapor absorb the latter until saturated. At room temperature this requires twenty-four hours, at the expiration of which the material exposed is completely sterile and remains so, showing that the micro-organisms have been not only inhibited but destroyed. Upon raising the temperature of the vapor to 45° or 50° C., sterilization is secured in half an hour; 55° C. should not be exceeded, as the formaldehyde then begins to decompose. The writers employ this agent for routine sterilization. The apparatus consists merely of metallic boxes, closing tightly, at a short distance from the bottom of which is a tray covered with powdered trioxymethylene; the latter, in turn, is protected with several layers of fine gauze, which prevent particles of the formaldehyde liberating powder from reaching the material to be disinfected when the box is heated. Surgical paraphernalia in daily use are sterilized with the warmed formaldehyde vapors, while other material is sterilized in the cold, being left in the box for forty-eight hours. Rubber gloves are in no wise injured by this procedure, as they are by boiling or steam under pressure. Instruments need not be boiled unless they have been used in septic operations. Suture materials not intended for resorption, and dressings, including protective silk, are easily sterilized without deterioration provided they are unrolled. Barthélemy performed 600 operations with all the materials used sterilized by formaldehyde, while F. Gross has done 1000 celiotomies and a like number of radical hernia operations with gloves thus treated.

The results, which were entirely satisfactory in these cases, lead the authors to recommend the method for widespread use, owing to its simplicity. Gross and Barthélemy (N. Y. Med. Jour., from Revue de chir., Jan., 1913).

Formaldehyde has the property of hardening nitrogenous substances of the nature of gelatin. This has been made use of in the preparation and sterilization of catgut. After this method of preparation the catgut can be boiled without destroying it.

THERAPEUTIC USES.—Gynecological Disorders. — In **vaginitis** and **catarrhal endometritis** a tablespoonful of a 10 per cent. solution of formalin to a quart of water has been found useful. In **gonorrheal vaginitis**, good results have been claimed from the use of formaldehyde. The vulva was washed with a 1:1000 solution, and the vagina douched through a speculum with a strong solution, varying from 2:1000 to 5:1000. If the uterine cavity and cervical canal were involved, a weaker solution was injected. When there is laceration of the cervix, tampons soaked in 1:1000 of formaldehyde are left for two or three hours in the vagina. When fungous endometritis is present, the curette must be first applied. The applications give rise to no pain, and may be used daily, or every second day.

General Surgery.—Though a powerful antiseptic, formalin has been little utilized in surgery, owing to the intense pain and irritation it causes when applied to the living tissues. When, however, an excess of hydrogen peroxide solution is mixed with formalin, a chemical reaction takes place which destroys the formalin and completely checks its irritating and pain-giving properties.

J. Clark Stewart (Surg., Gynec. and Obstet., Aug., 1911), taking advantage of this fact, applies the liquor formaldehyde, U. S. P., freely to infected wounds, leaves it in contact approximately one minute, and then neutralizes it by the use of hydrogen peroxide. It is important, he says, that an excess of hydrogen peroxide be used, in order that all formaldehyde shall be surely destroyed. If too little peroxide is used the chemical reaction is incomplete, and a certain amount of formic acid is produced, which is an irritant. From hospital and private experience with this mode of antisepsis, Stewart recommends it in the following clinical conditions:—

First, in **infected wounds**, it largely supersedes phenol followed by alcohol; it seems no more painful, and is decidedly more efficient. Wounds are thoroughly mopped out with the formalin, and after one minute or more if there is no pain an excess of peroxide is poured in, and the resulting foamy discharge wiped away. Often one such treatment will change an infected into a healthy wound, but in some the application must be repeated after one or two days. The coagulating and hardening action of the formaldehyde was not in evidence, owing probably to its neutralization.

Second, as a deodorant in **ulcerating carcinoma.** A 10 per cent. solution of formaldehyde applied by means of gauze on the ulcerating surface, the surrounding skin being protected by a thick covering of vaselin, will remove all odor and check discharges; but the author discovered that the pure formalin (officially 37 to 40 per cent. formaldehyde), controlled by hydrogen dioxide, answered the same purpose more quickly and with less pain.

Third, for the control of the fungus of **sarcoma,** with its troublesome hemorrhage and discharges. As soon as the fungus appears it is painted with formalin or cotton wet with formalin left in contact with it. If the skin is protected there is no pain, and the fungus is soon changed into a black, leathery mass. After the subjacent pressure has increased, the sarcoma will burst through the hardened portion, and the process must be repeated. In some cases the hypodermic injection of formalin very superficially around the base of the fungus seemed to improve the condition. Care must be taken, both in injections and in applications, not to allow any surplus to invade the unprotected skin. In one case treated for fungus in the groin, the fumes alone seemed to irritate the scrotum; protection must be provided.

Vesical and Urethral Disorders.—Lamarque recommends the use of a 1 per cent. solution for irrigating the bladder and urethra and a 5 per cent. solution in **chronic gonorrhea.** In **hematuria and tuberculous cystitis** it has also proved of value.

> Formaldehyde solution irrigations are especially valuable in **cystitis** associated with ammoniacal decomposition of the urine, such as occurs with enlarged prostate or tumor of the bladder. There are marked individual variations, however, in the tolerance of the vesical mucous membrane to formaldehyde, which are independent of the state of inflammation present. An acutely inflamed bladder is much more intolerant than a healthy one.
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> In **chronic cystitis** and in healthy bladders the writer found it practicable to use solutions varying in strength from 1:3750 to 1:7500. Occasionally a bladder was met with which did not tolerate even the latter solution, but no cases came under observation which would not tolerate a 1:12,500 solution.
>
> It was found the kidney pelvis, injected by means of a renal catheter, would tolerate solutions as strong as the bladder. No irritation in the kidney itself was ever noted after such an irrigation. C. F. Burnam (Arch. of Intern. Med,. Oct., 1912)

Ammonioformaldehyde was found by E. L. Keyes, Jr., to be almost a specific in some cases of uncomplicated **acute catarrhal pyelitis.** To prove effective it may have to be administered in large doses until the urine is practically free from bacteria, after which a smaller dose may be sufficient. In judging the effects of the drug the centrifuge and the microscope should be employed. The dose must not be sufficient to cause pollakiuria and dysuria by irritation of the neck of the bladder. The possibility of such an irritation cannot be overlooked even when small doses are given.

Cutaneous Disorders. — Poitevin suggests the application of a layer of absorbent cotton dipped in a 2 per cent. formalin solution and covered with an oil-silk or rubber bandage in parasitic diseases (**ringworm**) of the skin. Its vapors diffuse readily, even through masses of fatty matter, which makes it specially suitable for the treatment of deeply implanted diseased hair, and also for the disinfection of the hair-follicles filled with sebaceous matter. In case of irritation of the skin, the bandage may be removed for a day. It has also been recommended in cases of **psoriasis** and **lupus** as a local application.

Formaldehyde in free solution is very efficient as a wash in **fetid sweating** and in **colliquative sweats.** A proprietary preparation termed "enformol," which contains formaldehyde and aromatics, is preferable to the plain solution in that it is not unpleasant to the patient.

Insects are readily killed by weak solutions of formaldehyde, and an easy way to get rid of **flies** (which are increasingly being associated with infection) is to place 1 dram (4 Gm.) of the official liquor formaldehyde in a saucer of sweetened water, a solution which flies drink with avidity.

When a watery solution of gelatin is allowed to dry in formalin vapor the chemical characteristics of the gelatin are altered. It is no longer affected by hot or cold water, nor by acids or alkalies. Animal tissues, however, have the power of breaking up the combination and setting the formalin free. When the formalin-gelatin, ground to a fine powder and mixed with cultures of various forms of pathogenic bacteria, was introduced into animals, the bacteria did not develop, and the wounds healed without trouble. With this *formalin-gelatin powder* every **acute suppuration** can be stopped in twenty-four hours, and **wounds** made to heal aseptically.

Schleich has used it in **acute suppurative processes, aseptic wounds, compound fractures, deep scalp wounds** and other exposed lesions. The wounds were only cleansed mechanically, and then thoroughly rubbed with the powder. In cases of **necrotic masses,** in old **ulcers,** etc., the formalin-gelatin powder is dusted on the wound, and then covered with a dressing wet with the pepsin solution and the digestive process keeps up a continuous supply of formaldehyde vapor for the wound. The powder is made by drying 500 Gm. (16 ounces) of purified and dissolved gelatin in the vapor of 25 drops of formalin.

Schleich's formalin-gelatin was found of great value by Foote in the treatment of **suppuration,** giving the most perfect results in those cases where the cellulitis is moderate and the pus abundant.

Good results from local application of formaldehyde are reported by R. L. Hammond (Amer. Med., July, 1912) in **verruca** (warts), **clavus**, (corns), **callositas**, **nevus pigmentosus**, and **cornu cutaneum**. Formaldehyde of 40 per cent. strength was invariably used, undiluted; a wooden toothpick or matchstick was dipped in it and the adherent drop applied to the surface of the lesion, every three or six hours for two or three days. Care was taken not to touch the normal skin with the agent. After several days, in the case of small excrescences, and in about a week, with the larger ones, an application having been made three times daily, it was found that pain was experienced, devitalization of the tissue occurred, and, upon discontinuance of the applications, the growths desiccated. After exfoliation the under surface or dermal layer appeared free from the blemish, or, if not, another application or two secured the desired result. If an open sore is produced, the author adds, a healing ointment of zinc oxide or simple cerate is usually all that is needed. In the case of small excresences the applicator should be whittled to a fine point. In extensive callosities the remedy can be applied with a brush three times daily for several days, or until the surface becomes sensitive; then the applications should be stopped and the parts allowed to dry, when by soaking the epidermis with warm water it can be rubbed off. This process can be repeated until a cure is effected. In cornu cutaneum the horny growth should be clipped away as near to the dermal attachment as possible and the agent then applied as often and thoroughly as it can be with comfort. Formaldehyde exerts a local anesthetic effect; but this does not protect against its own irritating action. Large and **painful** warts were, however, removed by its aid with much less pain than attends their removal by other agents, such as nitric acid, zinc sulphate, etc.

Ophthalmic Disorders.—Formaldehyde has been recommended as a disinfectant in **ulceration** of the **cornea**, the solution generally preferred for **collyria** being 1:2000. Stronger solutions should be applied immediately to the seat of the ulcer.

Disorders of the Respiratory Tract.—In the treatment of diseases of the nose, larynx, and lungs formaldehyde has been recommended by a number of observers, in solutions ranging from 2 to 40 per cent. Although these reports merit credence, the fact remains that the irritation produced is such as to deter many from using it in preference to other means.

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FOURTH DISEASE.—This is an infectious disease first described by Dr. Clement Dukes in 1900. It is thought to be to scarlet fever what rubella is to measles. According to Cheinisse, it is identical with scarlatina variegata. The cause of the disease is unknown.

> It was not until the close of the seventeenth century that, mainly through the researches of Sydenham, scarlet fever ceased to be confounded with measles, and now, at the close of the nineteenth century, rose-rash is still confused with measles and with scarlet fever. Finally, on the verge of the twentieth century, it is being discovered that a fourth dis-

ease, perfectly distinct from measles, rose-rash, and scarlet fever, is to be distinguished. But whatever name for this disease should be ultimately adopted, it should obviously preclude any possible confusion with scarlet fever or rose-rash.

The question has occurred whether the fourth disease which so closely resembles scarlet fever would tend in a series of cases gradually to develop into true scarlet fever. But the slightest indication in this direction has never been observed. This is a well-expressed line of demarcation between the two diseases, and notwithstanding their close superficial resemblance every case is either the true fourth disease or true scarlet fever. Clement Dukes (Lancet, July 14, 1900).

SYMPTOMS.—The symptoms recall those of two diseases, viz., scarlet fever and German measles. The incubation period varies from about ten days to three weeks and prodromes are usually absent. The onset is usually abrupt, although malaise and sore throat are sometimes present. The rash appears suddenly, covering the body within a few hours. The face is oftentimes free from the rash. The latter is of a bright-red color and is followed by slight desquamation, although in some cases the desquamation is marked. There is usually a slight fever, the temperature rarely going above 101° F. and some glandular enlargement is present.

Summary of 19 cases of a series of this fourth disease: There were practically no premonitory symptoms and no illness was complained of until the rash appeared, but on inquiry admission of general malaise was elicited. In 1 case free vomiting occurred in the night and a very full rash was discovered in the morning. This vomiting arose, however from his having eaten freely of sweets in the evening. The maximum temperature throughout his illness was only 99.6° F.

The first symptom to attract the attention of the sufferer was the rash, which in nearly every case was very full and quite characteristic of scarlet fever. The fauces were red and swollen, but occasioned so little discomfort that complaint was rarely made, and the condition was only discovered on inquiry or inspection. In some cases the skin became merely rough; in most instances there was free desquamation of small scales; while in others the peeling was equal to the worst ever noticed in scarlet fever. In this fourth disease the desquamation bears no relation to the intensity of the eruption; several of these cases with the fullest and intensest eruption were followed by very scanty desquamation. The peeling may continue as long as in scarlet fever, although it is apparently innocuous. The tongue was furred throughout, which cleaned as all furred tongues do. In no case did the tongue peel on the fourth day, as is so pathognomonic of scarlet fever in both mild and severe attacks.

The lymphatic glands universally were enlarged, hard, and tender, sometimes excessively tender. The average temperature was 101° F. (38.3° C.), but it ranged from 99.4° to 104.2° F. (37.4° to 40.1° C.). The temperature almost invariably became normal on the third or fourth day. In only 1 case did the pulse reach 100—a signal contrast to the accelerated pulse of scarlet fever.

In no instance did albuminuria arise, although all the sufferers except 2 were fed freely as soon as the slight fever (which occurred from the third to the fifth day) had disappeared, and the boys were removed from bed as soon as the rash had subsided.

It was impossible to ascertain the incubation period in this series of cases, since several of them occurred simultaneously. It is believed the incubation varies from nine days to twenty-one days. The duration of infectiveness lasts from ten to fourteen days or even twenty-one days, where efficient disinfection is in operation. The continuation of desquamation is apparently of no moment as a cause of infection or sequelæ. Scarlet fever had not occurred previously in any instance. Eight boys had already suffered from rose-rash out of this series of 19 cases, or 42.1 per cent. Clement Dukes (Lancet, July 14, 1900).

The writer has been able to verify Duke's conclusions, and from his clinical experience noted that the disease usually lacked prodromal symptoms, with the exception of pain in the neck. In some of the more severe cases, however, there were noted for some hours headache, nausea, loss of appetite, pain in the back, and occasionally a chill. This agrees to rubella very well, but is in marked contrast to scarlet fever. The eruption is usually the first appreciable symptom which in the course of a few hours covers the whole body. This appears in the form of a small punctiform, thick beset, pale raw red, erythematous eruption that is not perceptible above the skin. It is also to be seen over the face, though here not so plainly. According to Dukes the lips and the dorsum of the nose are free. The pharynx is slightly swollen and injected. The cervical glands are hard and enlarged to the size of a pea. Occasionally the axillary glands and those of the groin are enlarged. The eruption is of short duration; the desquamation is fine and bran-like, lasting about fourteen days. Nephritis is seldom seen following the disease. The pulse is not rapid. The temperature ranges from 98° to 104° F. (36.7° › 40° C.), which is not increased during the eruption. On the fifth or sixth day the patient can usually be up and about. In fourteen to twenty-one days the danger of infection is passed. It seems as though various clinicians are divided in their opinions as to the condition being a disease entity or an abortive form of scarlet fever or rubella. Johnson and Bo Kay (Deut. med. Woch., Oct. 20, 1904).

DIAGNOSIS.—The disease must be differentiated from scarlet fever and German measles, and may occur with either of these diseases. There are no sequelæ.

> When one or more cases of apparent mild scarlet fever occur in a family giving a clear history of former attacks of scarlet fever, Dukes's disease may be suspected. Anomalous cases of doubtful diagnosis were exceedingly common during a recent epidemic of scarlet fever in Chicago, and many came to the writer's attention. There were but few cases of rubella, as we understand that disease. The health department reports represent less than one-fourth of the epidemic. Twenty-four physicians personally interviewed admitted having had 478 cases, though reporting only 117, the others being diagnosable only as suspicious. A. C. Cotton (Jour. Amer. Med. Assoc., Oct. 26, 1907).

TREATMENT.—The treatment is purely symptomatic. The **diet** should be light and nutritious. **Rest** in bed is essential, especially if there is much fever. During desquamation **cleansing baths** should be given and the **skin anointed with olive oil** or **cacao butter.** H.

FRACTURES. —DEFINITION.

—A break in bone or cartilage, either partial or complete, is known as a "fracture."

ETIOLOGY.—The active factor in the production of a fracture is some form of mechanical violence (external violence or muscular action). External violence may act as:—

A. *Direct violence,* in which case the bone breaks at the point upon which the fracturing force is received, and in this type more extensive injury to the soft parts occurs.

B. *Indirect violence,* in which case the bone breaks at a distance from the application of the fracturing force due to bending, torsion, or compression of the bony structure beyond the breaking point.

Muscular action acts directly by traction, as seen in the avulsion of the posterior portion of the os calcis; or, it acts indirectly by the action and counter-action of opposing muscles, as seen in fracture of the humerus produced by the act of throwing.

Predisposing Causes.—Sex, age, and occupation are remote predisposing causes of fracture. Men suffer more frequently from fracture than women, for they are much more often exposed to injuries of all sorts. Yet after the age of 70, women suffer many more fractures than men, chiefly of the neck of the femur. Again, while by far the greater number of fractures occur in the first three decades of life, the proportion of fractures *per capita* is at its maximum at about the age of 60. More definite predisposing causes, however, reside in the anatomical and pathological condition of the bones and the system in general. Normally, the shape, structure, and functions of various bones expose them more or less to fracture, the liability to which is increased by the changes incident to advancing years. The curves in the long bones and their broad, spongy ends, so well adapted to transmit the minimum of danger to more vital organs, render them, for that very reason, more liable to give way under excessive violence. Seventy-six per cent. of all fractures occur in the ribs, clavicle, forearm, hand, and leg, while the upper extremity, the weapon of offense and defense, receives 51 per cent. of the total. The middle-aged and the aged, while less exposed to trauma than the young, receive more than their share of fractures, partly because of their decreased agility, the normal stiffening of their muscles, but mainly on account of the normal changes in the osseous system. As age advances, the spongy and the compact tissues of the bones become gradually rarefied, not by any changes in the proportions of their bony constituents, not by any deposit of lime-salts, but by an actual diminution of the amount of the bone tissue. Such changes are pathological only when they occur at an early age. In a few cases an unlimited tendency to this early bone rarefaction has been observed.

Fractures of this kind usually heal kindly, and refracture through the line of union is the exception, although, in the more pronounced forms, the patient may scarcely have convalesced from one fracture before some slight accident disables him with another one. A similar bone fragility may be acquired through prolonged disuse or consequence of lesions of the nervous system.

Rachitis in children and in later days syphilitic bone lesions, bone tumors, and inflammations act as predisposing causes of fractures, and notably delay, if they do not entirely prevent, the process of repair. The existence of rheumatism as a predisposition is very doubtful, the pathological connection between the two not having been demonstrated, and the clinical history of "aches and pains" probably a mere coincidence.

PATHOLOGY.—Varieties.—1. Incomplete fractures.

(*a*) Fissure.
(*b*) True incomplete "green-stick" fracture.
(*c*) Depressions.
(*d*) Separation of a splinter or apophysis.

2. Complete fractures, subdivided according to

(*a*) The direction and character of the line of fracture,—as transverse, oblique, longitudinal, dentate, V- or T-shaped, and comminuted.

(*b*) The seat of the fracture, as fracture of the shaft of the neck, head, shaft, separation of the epiphysis, etc.

(*c*) If extending into a joint, intra-articular fractures.

3. Simple fracture—a closed fracture, one in which there is no open wound in the skin in contradistinction to—

4. Compound fracture—an open fracture, one in which there is an open wound in the skin communicating directly or indirectly with the line of fracture.

5. Gunshot fractures.

6. Multiple fractures—a term used when there is more than one fracture in a bone or when more than one bone is broken (not applied to forearm or lower leg when both bones are broken in those regions).

We need not concern ourselves here with the lacerations and the process of repair of the soft parts. As for the bone, it may give way more or less completely and in one or more places (see VARIETIES). If the fracture amounts to anything more than a simple fissure, the periosteum is torn and usually stripped up for some distance. As a general rule, however, it remains untorn at one side, thus forming a so-called "periosteal bridge"; a valuable adjunct to repair, and tending to insure the life of all fragments that remain attached to it.

The bones are displaced in six ways (Malgaique). These six primary displacements are:—

1. Transverse or lateral. 2. Angular. 3. Rotary. 4. Overriding. 5. Impaction or crushing. 6. Direct longitudinal separation.

Displacement is caused by the combination of the trauma and the action of the muscles attached to the fragments, and the actual displacement is usually the result of a combination of several of the original ones.

If the displacement is considerable and the bone-ends angular, a great deal of damage to the soft parts may result from injudicious handling, a secondary compounding of the fracture being a not infrequent result of carelessness in manipulation and transportation, especially in fractures of the leg.

Bullet Wounds.—Recent researches are tending to clear up the mystery surrounding the contradictory reports on the effect of modern projectiles. A slowly moving bullet, one almost spent, if it strikes a bone will bore through it more or less completely and splinter it more or less widely in a manner that can be explained by the velocity, the angle of impact, and the quality of the bone; but with a swiftly moving, small-caliber bullet, another force has to be considered,—that of vibration. If the vibration imparted to the bone by the projectile is such that the point of impact of the projectile coincides with a nodal point, the bullet will simply pierce the bone and no shattering will result. But if the point of impact does not coincide there will be more or less shattering at the point and at the extremities of the bone, the amount of shattering being dependent on the amount of vibration imparted to the bone. Now, the qualities in the bullet that tend to produce vibration are its momentum (weight and speed), which is imparted more or less to the bone as the bullet is larger or smaller and as its point is harder or softer. Consequently the shattering power of a bullet increases with its velocity, its weight, its size, and its capacity to flatten out when it strikes a hard object.

In bullet wounds of the cranial cavity, and to a less degree of the thoracic and pelvic cavities, the amount of damage is, again, often dependent on the vibrations produced, the waves set up by the passage of a solid object through a semifluid medium, more or less hermetically sealed within an unyielding envelope. Whereas the even passage of the bullet does comparatively little damage, the waves of motion it produces may suffice to literally blow the top of a man's head off.

The Process of Repair.—The first attempt at repair is seen in the periosteum, which throws out a layer of granulations. These become cartilaginous and finally bony, being the only portions of the callus to pass through a cartilaginous stage. The bone and marrow also share in the separative process, but to a less extent. They throw out granulations, which combine with these from the periosteum to fill the whole space between the bone-ends, even the medullary canal (forming the so-called "medullary plug"). The bone acts more slowly than the periosteum on account of the relative scarcity of its cellular elements, and because it has the added task of dissolving and making away with the thin layer of bone substance which is infallibly destroyed at the point of fracture. The callus thus thrown out forms a large, irregular mass, whose size is increased in proportion to the degree of displacement, the amount of comminution, and the lack of immobilization. If the callus is thus rendered unduly large, it may involve adjoining tendons, nerves, or joints, thus complicating recovery. If the line of fracture runs into a joint, it may become permanently immobolized by osseous union of its articular surfaces.

Fragments detached fom the periosteum may regain their vital connections by revascularization of their Haversion canals, or they may remain imbedded in the callus as innocuous foreign bodies. In this condition they may ultimately lead to suppuration.

If the vital energy of the bone-forming elements is not sufficient to form bony union, the callus remains fibrous. The usual causes of fibrous union are systemic debility, separation of the fragments, faulty immobolization, and the presence of foreign bodies,—*e.g.*, wire sutures.

Ultimately the medullary plug is absorbed and the callus becomes entirely bony, shrinking, in cases that have been completely reduced, almost to a simple layer between the bone-ends, any sharp angles of which are also gradually rounded off by absorption.

Repair of Compound Fractures.—If they heal by first intention their repair follows the same course as that of simple fractures, but when suppuration occurs partly detached fragments that would otherwise have lived are cast off, and the ends of the larger fragments also die, and act often for long periods of time as foreign bodies to which sinuses run, after all active suppuration has ceased. In such cases the dead bone should be cut down upon and removed. After suppuration none of the callus goes through a cartilaginous stage.

SYMPTOMS.—Deformity.—Under this head are included all the changes in appearance and dimension of the injured part. Some deformity is always present, dependent upon the contusion or laceration of the soft parts, or, what is much more important, the displacement of the bone-ends upon each other. Most of the various displacements can be recognized by the eye or finger, but if the seat of the suspected fracture is covered by a thick layer of soft tissues, and especially if the contusion of these soft parts has given rise to a considerable amount of superficial deformity, mensuration must be resorted to. Measurements are best taken from bony points at opposite ends of the bone whose fracture is suspected, and the shortening or lengthening ascertained by comparison with the distance between the corresponding points on the opposite side of the body (*e.g.*, the sound limb). Unfortunately, however, it is often impossible to take measurements with any degree of accuracy from two points on the same bone, consequently the rule that must always be borne in mind, viz., for a comparison of the measurements of the sound and the injured limb these measurements must be taken with the limbs in not apparently, but really corresponding positions. Two other sources of error are: first, that the length of limb in some subjects is normally asymmetrical; and, second, that previous disease may have affected the length of some one of the bones measured. Circumferential mensuration of a limb is valueless, for the increase in circumference of the injured limb, in cases where the bone deformity cannot be readily made out, is usually due more to the effusion of blood into the soft parts than the overlapping of the bone-ends. The deformity of the soft parts is such as is caused by whatever contusion or laceration they may have received. Generally speaking, the swelling increases for twenty-four to forty-eight hours, and then gradually subsides, its subsidence being hastened by treatment: a fact which is of the greatest importance in reference to the application of splints.

Abnormal mobility and crepitus are the two other objective symptoms of fracture and are pathognomonic. In exposed positions the former sign may be elicited by directly grasping the segments of the bone and moving either upon the other; in other cases (fracture of the surgical neck of the humerus) the surgeon must be satisfied with determining that the motions (rotation) of one fragment (the shaft) are not imparted to the other, as indicated by the immobility of one of its bony points (the greater tuberosity). Again, abnormal mobility near a joint may simulate abnormal mobility of the joint itself, and special care be necessary to differentiate between fracture and dislocation.

Crepitus is the grating sensation heard or felt when the two rough bone-ends rub against each other. The intervention of soft parts between the bone-ends, of course, prevents crepitus, which may, on the other hand, be simulated by crackling of coagulated blood, by roughened joint surfaces, by tenosynovitis, and by emphysema. Finally, be it especially noted that although abnormal mobility and crepitus are pathognomonic, they are often by no means necessary to the diagnosis of fracture, and the manipulations which they require may be not only extremely painful, but also, by producing further lacerations of the soft parts, positively harmful to the patient.

Loss of function is usually present to a greater or less degree, and is due to the weakness of the part or to the pain evoked by motion or pressure; but this symptom is liable to be misleading, for, while one patient may use a fractured limb with great freedom, another may be totally disabled by a mere contusion. In the long bones and about joints the deformity is usually increased by active motion.

> In shaft fractures fixation is of first importance; in joint fracture the main object is to secure good function and preserve good alignment of the limb as a whole, and avoid local deformity and non-union as far as possible. We do not need the massive hardware so often used in shaft fracture; a chromic gut or wire suture, or a steel pin or staple is generally enough, and often these are not needed. Replacement of fragments is the first thing, but accurate reposition is usually impossible except by an open operation, and many a joint works well without this. Non-union is often a bugbear, but the presence of synovial fluid, preventing clotting and the formation of callus, is an important cause, and the solution of the problem of union in joint fracture is to exclude synovial fluid and to insure callus by securing contact. Opening the joint and draining into the tissues removes the bar to the formation of callus. F. J. Cotton (Jour. Amer. Med. Assoc., July 20, 1912).

Pain is always present except in unconscious patients. It may be elicited by direct digital pressure over the line of fracture, in which case it gives a very fair idea of the location and the line of fracture, or it may be elicited by indirect pressure, *i.e.,* by crowding the two fractured ends together by pressure against the distal portion of the injured part. In the latter instance the patient will localize the point of greatest pain at the site of the fracture.

Pain may also be elicited by voluntary motion of the injured part against resistance, in which case the pull of the ligaments and muscles by a mechanism of "cross-strain" will cause the patient to localize the maximum point of pain in the region of the fracture.

The evidence thus obtained, together with a history of injury, is often sufficient evidence of a fracture. Certainly no case presenting such pain so definitely localized to a given point should be treated otherwise than as a fracture.

Clinical Picture.—Immediately after the accident the torn vessels pour out their blood into the tissues, and within a few hours edema sets in on account of the occlusion of the lacerated veins and lymphatics and the obstruction of others by the pressure of the extravasated blood. The temperature may rise a degree or two, blebs appear on the surface, and the tense skin becomes discolored by ecchymoses. The discoloration which may appear a few days later, as the blood extravasated among the deeper tissues makes its way to the surface, perhaps at some distance from the point of fracture, is a presumptive sign that a bone lesion exists. In from one to five days—more rapidly under appropriate treatment—the edema subsides and the swelling is reduced to a hard lump, the mobility of the fracture becomes less, crepitus is no longer obtainable as the fractured bone-ends become covered with granulations, and, finally, after a few weeks abnormal mobility entirely disappears and the fracture is said to be united. But the patient is not yet well. Disease has stiffened the joints and weakened the muscles so that several weeks or months will be required before the limb regains its usefulness, while in cases where the proper care of the joints has been neglected they may remain permanently stiffened.

Children are peculiarly liable to subperiosteal fracture and the kind known as green-stick fracture. Roentgenoscopy is sometimes the only means for detecting the former. The green-stick fracture is often an unsuspected cause of coxa vara. The fact that the child is able to walk on the injured leg apparently excludes the idea of fracture. In a typical case of the kind a child broke its arm in a fall, but was able to walk, and the simultaneous injury of the neck of the femur was not suspected until walking became more and more difficult in a day or so.

Fracture of the ulna, when it occurred a little above the middle of the bone, was always accompanied by dislocation of the head of the radius in the 86 cases of the kind compiled by Perrin in 1909; all but 34 were in children, and the left arm was generally the one involved. One of the author's patients was only 33 months old. The head of the radius should always be examined in such cases; with simple fracture of the forearm there is very rarely any considerable swelling above, and consequently any tendency to protrusion above should suggest dislocation of the head of the radius. Kirmisson (Presse méd., Sept. 4, 1912).

DIAGNOSIS.—The degree of fracture should always be made with the least possible manipulation. A consideration of the patient's history, together with careful inspection, gentle palpation, and accurate measuring will usually suffice. If not, gentle manipulation of the injured part may be made use of for the purpose of eliciting abnormal mobility or crepitus. To this end general anesthesia is of great assistance by relaxing muscular spasm and removing pain; but with these safeguards against further laceration thus removed, manipulation should be doubly gentle. Moreover, a slight, gentle movement will often be of service when a brusque or violent one will fail.

The X-ray.—Since the advent of the X-ray sufficient data have been collected to show that an X-ray picture is not, in the large majority of cases, essential for the diagnosis of a fracture, but is an invaluable aid in determining the result of any given method of reduction and retention, and for the latter purpose should never be omitted. Certainly no delay in reduction should be permitted in order to obtain a radiograph.

In crushing injuries of the hand or foot, in fractures about the hip and shoulder, fractures of the pelvis, and in some injuries to the ankle-joint the X-ray is most serviceable in making a diagnosis, since the real bone lesion may be obscured by swelling or by the difficulty of finding any serviceable landmarks. In this type manipulation may only cause us to suspect a fracture, while the X-ray picture will, in the hands of experts, give a very clear idea of the bone lesion.

Differential Diagnosis.—Dislocation.—In dislocations there is restricted motion where there was motion before. In fractures there is motion where there was none before. Moreover, if, in dislocations the range of motion is increased in one direction, it is usually diminished in the opposite direction, while a fracture usually gives abnormal mobility in all directions. Crepitus is pathognomonic of fracture.

> Clinically, the history of sufficient injury with a small, sharply localized area of swelling and acute tenderness over a region of tendonous or ligamentous attachment is diagnostic of sprain fracture, and should be considered as such whether or not X-ray verifies the diagnosis. Tenderness of lesser degree may surround an acutely tender area. Tenderness lasts, as a rule, from five to twenty days, longer in improperly treated cases; however, those few cases with symptoms as given above, in which tenderness disappears within forty-eight hours, are, nevertheless, sprain fractures. The acute tenderness referred to is unmistakable; when the spot is firmly pressed on, the patient invariably winces. The following conclusions are reached: History of sufficient injury, with a sharply localized area of swelling and acute tenderness over a region of ligamentous or tendonous attachment, means sprain fracture. X-ray is not essential for the recognition of sprain fracture. The external malleolus is probably the most frequent seat of sprain fracture. About 15 per cent. of all fractures are sprain fractures. That condition formerly called severe sprain is sprain fracture. The condition resulting from stretching of soft parts is better termed strain. Sprain fracture is probably a part of the pathology of every dislocation. The case should be treated as a sprain fracture. Ross and Stewart (Annals of Surg., Jan., 1912).

In dislocation the head of the bone is in an abnormal poition, *i.e.*, the bony relationship of the articular surfaces are disturbed.

Contusion.—Position and pressure for a few days ought to reduce the swelling of the soft parts sufficiently to permit a satisfactory examination. Contusions of the hip form the exception. If even the X-rays fail to clear up the diagnosis satisfactorily, the only safe treatment is that for fracture.

PROGNOSIS.—The prognosis depends on many conditions, the extent of the injury, the associated lesions, and the age and general condition of the patient. Again, the prognosis for certain fractures (clavicle, Colles's) is far better than for others. Among the accidents that may imperil the patient's life are *embolism* of a clot from an injured vein into the heart or lung, causing instant death (see Embolism), or *fat-embolism,* a very rare condition which occurs during the first few days after fracture. The symptoms may be those of embolism or shock, or there may be more or less characteristic signs of edema of the lungs. Post-mortem examination reveals the fact that the pulmonary capillaries are obstructed by minute globules of fat, which have been poured into the gaping vessels from the torn bone-marrow. If the patient recovers, the diagnosis of fat-embolism cannot be made with any certainty.

Shock is a frequent cause of death, which usually occurs within the first forty-eight hours, and in compound fractures death may occur from hemorrhage, or later from tetanus or septicemia or pyemia. Delirium tremens is a frequent complication. The shock, the withdrawal of customary alcoholic stimulation, and the confinement to bed all tend to induce it. Besides the customary administration of hypnotics, stimulants, and nourishment, it is of the greatest importance to get such patients up and about while they are still in the premonitory stage of restlessness and insomnia. They must be gotten out of bed at any cost. I have seen this expedient succeed in abating an attack of delirium tremens when all other means bade fair to fail. Finally, gangrene may result from laceration of the main vessels of a limb or from their compression, whether by the displaced fragments or by a splint unskillfully applied.

Local sloughing of the tissues may occur from the pressure of a sharp point of bone, or, more commonly, by extravasated blood. The reduction of the fracture, followed by the application of heat and pressure and the elevation of the limb, constitute the elements of prophylaxis in such cases, to which must be rarely added incisions for the evacuation of clots or the ligature of bleeding points.

Other early complications are the secondary compounding of the fracture by a sharp point of bone, and the formation of a traumatic aneurism in a lacerated artery.

Complete recovery may be delayed or prevented by exuberant, painful, or weak callus. The callus always is "exuberant" at first, and may be expected to grow somewhat smaller even after bony union has taken place, but experience has proved that large masses of callus that impair function will not disappear in the course of nature nor under any medical, mechanical, or electrical treatment. They must be exposed and chiseled away, and in this connection it is well to remark that in old cases it may be impossible to tell before operation whether the offending mass is a badly reduced fragment or exuberant callus. Persistent pain in the callus may be due to pressure on a nerve or the inclusion of nerve-filaments in the callus, or to suppuration about a sequestrum.

Weakness of the callus, when it is not caused by undue separation of the fragments or constitutional debility, is usually due to inefficient immobilization. It is not an uncommon consequence of suppuration in a compound fracture.

Stiffness of the joints is, to a certain extent, the natural result of the immobilization necessary to secure union in the fracture. But this stiffness should be transitory except in the old and rheumatic, or unless the joints are sprained or involved in the fracture. In this last event permanent bony union of the apposed bone-surfaces may occur, or exuberant callus may interfere with the movements of the joints. The joints of the fingers, however, are very liable to remain stiff if they are immobilized for more than two weeks, especially if in the position of extension.

Atrophy of the muscles may be permanent in old and debilitated persons. In whom also spontaneous dislocations and fragility of the bones may result from disease.

Tumors—primary sarcoma and secondary carcinoma—may occur at the seat of fracture, and secondary carcinoma may occur in the epithelium lining of the old sinuses of compound fractures.

Permanent paralysis may result from laceration of or pressure on the nerves.

TREATMENT.—The treatment of any given fracture must vary with the type of the fracture, but in all cases the result to be desired is a restoration of function as near that of the normal function as is possible under the existing conditions.

The first essential in the treatment of all fractures is rest of the fractured area, and this rest should be secured at once on the spot at the time of the injury by some handy form of fixation to allow for the transportation of the patient to a place suitable for carrying out the detail of fracture treatment. Binding the arm to the body, bandaging the two legs together, the use of branches of trees, pieces of wood, etc., may be mentioned for this purpose. Hasty attempts at reduction under unfavorable conditions result in failure to bring about proper reduction, and cause the patient unnecessary pain, and may also cause a simple fracture to become compound.

When confinement to bed is necessary the bed should be narrow (a single iron bed), the mattress firm and any sagging of the mattress due to the weight of the patient should be prevented by placing a board or boards which should rest upon the sides of the bed, *beneath* the mattress.

With the patient under favorable conditions the next step in the treatment, unless associated injuries or shock demand instant attention, is the reduction or setting of the fracture. Excessive subfacial swelling and impaction without development are contraindications to immediate reduction. Obviously many fractures, such as fractures of the ribs, require nothing but immobilization. Reduction may be done by manipulation, by open operation, or by various types of traction apparatus, and a judicious selection of the method of reduction is a primary essential for a favorable result.

If reduction of the fracture is impossible after the use of morphine hypodermically, a general anesthetic should be used. The nature of that anesthetic must of necessity vary. Nitrous oxide and oxygen, ether, and chloroform must be chosen or rejected for the same reasons as exist in the general field of surgery. In children a satisfactory reduction cannot be obtained without an anesthetic.

> Lerda and Zuenn have been very successful in reducing and treating fractures without pain by means of local anesthesia with a ½ of 1 per cent. **cocaine** solution. His own results in 50 cases of subcutaneous fractures and dislocations have been equally satisfactory. His method consists in injecting a 1 per cent. **novocaine-suprarenin solution,** the pain subsiding in a few minutes and remaining absent for a considerable time. In 3 cases of fracture of the radius where 10 c.c. of the anesthetic solution were used, reduction was unattended with the least pain, while in 7 cases of fractures of the forearm the method of plexus anesthesia produced complete muscular relaxation and loss of sensation. Backward dislocation of the forearm, as well as supracondylar fracture of the arm with dislocation, could be reduced without the least suffering. In 15 cases of luxation of the shoulder-joint plexus anesthesia was employed ten times and interarticular injection in 5 more recent cases. In making the latter 10 c.c. of the novocaine-suprarenin solution were injected just beneath the acromion into the joint and another 10 c.c. down to the head of the humerus, which was located below the clavicle. The author also reports favorable results in fractures of the ankle, leg, and knee, and in dislocations at the hip-joint. No deleterious effects were ever observed. H.

Braun (Deut. med. Woch., Nu. 1, 1913).

Certain types of fracture are particularly suitable for immediate reduction by manipulation, of which one may mention Colles's fracture, Pott's fracture, fractures of both bones of the forearm and leg, fractures of the clavicle, etc. Careful palpation will readily determine the position of the fragments and, by using the more superficial bone as a guide, one may determine fairly accurately the degree of reduction obtained.

Reduction by traction may be used, as (1) Traction by weight or weight and pulley (see Buck's extension). (2) Traction by suspension (Hodgen's splint or vertical suspension. (3) Traction upon specially made nails driven into the lower fragment and to which the extension weight is fastened (Stinemann "nagel extension").

Every limb to which adhesive plaster is to be applied for purposes of traction should be shaved, wiped with alcohol, and the adhesive plaster applied. Traction should then be made with a sufficient degree of abduction and flexion to bring the limb into proper alignment and maintained by a weight sufficiently heavy for that particular case. The more rapidly extension is produced the better; therefore heavy weights should be used early.

The result of such traction should be controlled by daily measurement, palpation, adjustment of the alignment, and by an X-ray picture with the traction apparatus and its accessories in action during the radiographing of the fractured area.

If the above procedures show measurements and alignment practically identical on both sides too much stress must not be placed upon minor degrees of displacement as shown by the X-ray. Should the traction not bring about the desired reposition in a week or ten days, it should be discarded.

Open operation is indicated in fractures of the patella and olecranon with separation of the fragments, and in fractures which cannot properly be reduced by other methods, or in articular fractures when the displacement if uncorrected may seriously interfere with the motion of the joint.

> Operative treatment is only indicated after the exhaustion of all rational non-operative means. A conscientious practice of the rule of exhausting the non-operative means of reduction will obviate the necessity of operation in many so-called irreducible fractures. There are, of course, certain indications for the open treatment which all recognize and follow, unless they are outweighed by equally positive contra-indications. In the first place, the situation of the bone or the type of the fracture may be a sufficient indication for operation; this is the case in fractures of the patella, in many fractures near a joint, in an epiphysial separation which cannot be perfectly reduced, in some comminuted fractures, in those where a muscle or tendon or other tissue is interposed between the fragments, where a nerve-trunk has been caught under one of the fragments. J. H. Gibbon (Annals of Surg., March, 1912).
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> The method of treatment which offers the patient the most satisfactory functional result with the least danger should be the method of election, that the future will show that the methods which most nearly fulfill these requirements are the non-operative methods of reduction. The more experienced the profession becomes in the handling of fractures, the better the results. Operation must be considered, not the method of election, but of selection for a care-

fully chosen group of cases, and in selecting the types for operation each case must be considered a law unto itself. Many cases of the various types of fractures are reviewed, in which non-operative treatment was employed, and in only a few cases were the results not entirely satisfactory. Hitzrot (Annals of Surg., March, 1912).

In the last two years out of 2100 patients 104, or 5 per cent., have been operated on in the Roosevelt Hospital. Increase in range of motion and decrease in deformity to be gained by the open method do not warrant the risk of operation. Most fractures are best treated by the closed method. Where a satisfactory reduction cannot be obtained and maintained by the closed method the fracture or dislocation should be treated by the open method, there being no other contraindications. If an open reduction is done, as simple and as little foreign material should be left in as possible. The decision to operate should be made before the eighteenth day, and earlier if possible. In old cases it is often better to do a non-reducing operation. The technique cannot be too exaggerated. An open reduction is a serious operation. It should only be undertaken with clear indications and with the most favorable operating facilities and surroundings. It must not be forgotten also that the open method is not always successful. H. Darrach (Jour. Amer. Med. Assoc., Aug. 3, 1912).

After an experience with open operation in 22 cases of fracture of various bones the author concludes that, especially in the treatment of fracture of the shaft of the tibia, in which fracture it is difficult by conservative methods to replace the fragments or to keep them in position once they have been replaced, the open operation with fixation by means of plates and screws is highly to be recommended. Also, in fractures of the femur which show no tendency to healing, or which have healed in very bad position, open operation gives very satisfactory results. Fractures of the humerus with marked displacement at points well removed from the joints afford a suitable field for this form of operation. In fractures close to the elbow-joint bone suture will always remain a two-edged sword. So far as the ulna, the olecranon, and the patella are concerned, the author has had better results with suture than with plates and screws. Frankenstein (Deut. Zeit. f. Chir., Bd. cxiv, Heft 1-3, 1912).

The committee of the British Medical Association reached the following conclusions: (1) In children non-operative treatment of fractures of the long bones except of both bones of the forearm yields as good results as does operative treatment. (2) In comparison with non-operative results in children the results of similar treatment in those past childhood are not satisfactory. (3) As age advances there is a progressive depreciation of the functional result of non-operative treatment. (4) This effect of age is less marked in cases treated by immediate operation. (5) Only the method which definitely promises a good anatomical result should be accepted as the method of choice. (6) Functional results may be good even with an indifferent anatomical result. (7) Operative treatment should not be regarded as a method to be used after the failure of the non-operative, as the results of secondary operations are very unfavorable compared with those of immediate operations. In order to secure the best results, operation should be undertaken as soon after the accident as practicable. (8) Operative treatment of fractures requires special skill and experience. It is not a method to be undertaken by any except those who have constant practice and experience in surgical procedures. (9) A considerable proportion of the failures of this method of treatment are due to infection of the wound, which may occur even with the best technique. (10) The mortality is so small that it cannot be urged as a sufficient reason against operative treatment of simple fractures of the long bones. (Brit. Med. Jour., Nov. 30, 1912).

Operation should not be undertaken except by an experienced surgeon, and then only in surroundings conducive to the most rigid asepsis.

> Death in 2 cases of operative fixation of fracture of shaft of femur. The first was that of a man, aged 50, with an alcoholic history, who sustained a fracture below the trochanters which was difficult to treat by apparatus. Two days later two metal plates were applied to the bone after exposure through an 8-inch incision. The apposition was obtained by traction exerted by compound pulleys. Suppuration of the wound occurred, and the man died of chronic sepsis complicated with alcoholic delirium about nine weeks later. Another man, aged 60, in good general health, with no alcoholic history, was operated for comminuted fracture involving the shaft of the femur below the trochanters and the neck. One plate was used to hold the main fragments in position. The operation was done eight days after injury. The patient died of chronic sepsis twenty-one days after operation. Pus was found in the medullary canal and among the muscles. J. B. Roberts (Jour. Amer. Med. Assoc., June 22, 1912).

The time at which the operation can be performed to best advantage is either immediately after the injury or preferably from five to nine days after the injury.

So many successful expedients have been proposed for the fixation of the fragments in open operations upon fractures that the individual selection of the type of fixation obviously varies.

No fixation is necessary when the two fragments can be held in alignment without it. Only strong catgut or kangaroo tendon is necessary in cases with slight tendency to displacement. In cases in which the above two procedures are not suitable the metal plates introduced by Lane are the most expedient.

> Smaller and lighter plates must be used if a tissue tolerance to them is to be cultivated. Removal of a plate is a matter of comparatively slight significance when restoration of anatomical and functional perfection are considered. The writer had not had to remove wires, nails, or plates where aseptic healing had been effected. Nothing short of absolutely perfect approximation, in his opinion, justifies an open operation for fracture. By this is meant a union so exact that no fracture line can be seen by spectators a few feet away from the field. An ideal result is possible even when Lane's plates are used in the presence of pus. Bartlett (Ills. Med. Jour., April, 1912).
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> In 60 cases under the writer's care, in which 66 platings were done, there was 1 operative death, 1 death from postoperative pneumonia, and 2 from sepsis. There were 26 perfect results. The greatest danger is from infection and consequent osteomyelitis. He advises the removal of the plate as early as possible in all platings of compound fracture of the tibia, fibula, radius, ulna, and clavicle, and cautions against placing the plate immediately beneath the skin. Plating is the most successful in simple fracture of the humerus and femur, if strict asepsis is observed. The writer advises the application of a snugly fitting cast immediately after plating; this requires as much attention as the plating. He uses plating only in cases in which the skigraph shows that it is clearly indicated; infection will occasionally creep in. Babler (Jour. Amer. Med. Assoc., May 25, 1912).
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> The writer employed every form of plate except the steel. In eleven years of practice on hip-joint cases he put on the pulley extension and got union in every case. He used the X-ray to watch the growth of union. We should use Lane's own method to do this sort of work to get results. Out of 100 cases 72 were perfect union and only 3 plates had to be removed, because he used Lane's method. A. J. Ochsner (Trans. Amer. Med. Assoc., N Y. Med. Jour., June 15, 1912).

Intramedullary splinting, fixation by screws with plates outside the skin, nailing the bone into place, etc., are recommended.

> The writer advocates the use of intramedullary bone pegs in the treatment of fractures for the following reasons: (1) The operation is easily and quickly performed and requires only a very small incision and exposure of the soft parts; (2) there is a minimum of injury to the periosteum; (3) the fragments are held in correct position; (4) slight movement is permitted between the ends of the fragments, thus stimulating rapid union; (5) extension splints are not needed after operation, and massage and passive movements are very easily carried out. In animal work he has tried several materials for the pegs and has found that magnesium is the best because it undergoes slow absorption with resulting marked stimulation of callus formation.
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> From the above observation the writer is led to believe that it may prove serviceable in man in cases of delayed union. Groves (Brit. Med. Jour., Oct. 26, 1912).

Splints.—Retention after reduction is usually maintained by some form of splint. For all practical purposes only three types of splints need consideration, namely, wooden splints, molded plaster splints, and circular plaster encasement.

Wooden splints should be long enough to include the proximal and distal joints, wide enough to prevent compression of the limb, and sufficiently padded to prevent pressure upon the skin, especially over bony points.

Molded plaster splints (introduced by Stimson) conform most readily to the demand for proper fixation, strength, lightness, case of inspection and removal. They are made by measuring the desired length with a piece of bandage (Canton flannel). Upon this the ordinary roller plaster bandage is carried back and forth, carefully smoothing each layer of the bandage as it is laid until the desired thickness is obtained (care should be taken not to make the splint too thick). While still plastic the splint should be molded to the limb and bandaged into place, avoiding circular turns of the retaining bandage. The splint rapidly hardens and, if properly made and applied, will maintain the most efficient fixation. All that is necessary for inspection of the fracture is the removal of the bandage, for, when hard, the splint readily keeps its postion—with very little assistance during the process of inspection.

Circular plaster encasement is still the favorite method with many. Its application must be made smoothly without compression and all bony projections well padded along the sides so that pressure will not come upon the skin over the bone. The toes and fingers must always remain exposed. After its application the fingers and especially the toes must be carefully watched and, if they become cold or blue, and the patient complains of pain, the cast must immediately be removed. Gangrene of the leg may result if the above is not done.

If circular plaster is used many writers advise cutting down the front of the cast while it is still wet and before the plaster has hardened. When the plaster has become firm the cast is held closed by an ordinary roller bandage wound about it.

Adhesive plaster is used in certain fractures for purposes of fixation (*vide* FRACTURE OF RIBS, CLAVICLE, etc.).

After-treatment.—Massage should be begun as soon as the callus is solid enough and as soon as pain on handling has disappeared, *i.e.*, about the end of the second week. This should include the whole extremity and gentle passive movements of the neighboring joints should be done at the same time.

> The value of early use of **massage** and **passive motion** in the treatment of simple fractures, is shown by the writer's 400 cases treated by this method with great success. Massage and movement should be considered as an essential part of the treatment of simple fractures. Since it allays pain, rapidly removes effusions, and improves nutrition, while movements of the joints prevent adhesions, these procedures cannot be commenced too soon—indeed, they are of most service during the first few days following the injury. Massage renders reduction and retention in good position easier. The method is exacting in time and skill, but is more comfortable to the patient, and insures a better and quicker return of function. Pirie Watson (Edinburgh Med. Jour., Oct., 1912).

In fractures involving the joints passive motion should be used, carefully bearing in mind the fact that such motion should be well within the limits of pain. It should never be forced. Forcible movement under an anesthetic should never be done. In general, the earlier **active** and **passive motion** is allowed, within the limits of pain, the better the result. Obviously no weight should be borne by a bone or bones which are not yet solid, without additional external support.

Baking with dry heat (160° to 300° F.) for one-half hour daily is a great aid in treating the joints. **Electricity** for the preservation of muscle and bone activity should be used more frequently than at present. Both the baking and electrical treatment may be begun at the end of the second week.

Compound Fractures.—If the wound leading to the fracture is small, clean, and not contused, as is usually the case, in compound fracture by indirect violence, the wound and any projecting ends of bone should be thoroughly cleansed, the skin painted with the tincture of **iodine**, the fracture reduced with as little enlargement of the external wound as possible, the wound loosely sutured, and primary union expected. In case the wound heals aseptically the course is that of a simple fracture, but, if suppuration sets in, the wound must be promptly opened up, thorough drainage provided for at dependent points, after which the healing is concluded under local treatment appropriate to granulating wounds.

If, on the other hand, suppuration has already set in or seems inevitable from the contusion or the dirty condition of the tissues, provision must be made at once for thorough drainage. The skin should be painted with tincture of **iodine** and the lacerated wound filled with **balsam of Peru** or an **iodine-guaiacol solution** (iodine, 1; kali iodide, 2; guaiacol, 5; glycerin, 100).

The latter is preferred. After such treatment a bulky dressing should be applied and the part put at rest. The guide to the investigation of such a wound is the temperature. If the temperature remains low (101° F. or lower) the wound had better be left untouched for from five to seven days. Of course, in the presence of evidences of existing suppuration, the surgeon may not hesitate to institute the most vigorous antiseptic treatment, but in doubtful cases the disturbance incident to frequent changes of dressing will certainly result in suppuration, while the expectant treatment may have a happier issue.

The necessity of removing detached fragments of bone depends almost entirely upon the prospect of suppuration. In a clean wound fragments that are entirely detached may lie, while in the presence of pus even the ends of large fragments will be cast off.

To estimate the amount of sloughing that will occur Esmarch's artificial ischemia is a safe guide, those parts being doomed to which the blood does not flow on the removal of the bandage. But it is inadvisable to attempt any extensive clearing away of dead tissue until the bone has begun to granulate and the line of demarcation has formed.

The suture of periosteum, fasciæ muscles, nerves, and tendons and the ligation of bleeding vessels merit no especial notice here.

As to the indications for resection or amputation, no definite rules can be laid down. In cases of doubt, however, it is always safe to delay amputation until it is clearly impossible to save the limb. Thus the patient is given every chance and the surgeon may avoid being sued for malpractice.

As to suppurating compound fractures of the larger bones they need almost never be despaired of, from twelve to eighteen months being none too long for their ultimate and satisfactory recovery.

> The successful treatment of compound fractures depend upon three principles: asepsis, drainage, and proper fixation or immobilization. There is more or less destruction and laceration of the soft parts, and more or less extensive fragmentation and comminution of bone. The vascular supply is interfered with on account of laceration or tearing of blood-vessels, resulting in a large outpouring of blood and serum. These wounds are therefore highly susceptible to infection. Primary drainage is required in these cases, supplemented by efficient counter drains as soon as indicated. The resort to secondary drainage is often imperatively demanded and must be ample because infection, which is now established, urgently requires the relief by the immediate and complete removal of all infectious matter and secretions resulting from bacterial activity and tissue destruction. C. H. Blickensderfer (N. Y. Med. Jour., Feb. 8, 1913).

Pseudarthrosis, or Delayed Union.—When on account of a constitutional taint (*e.g.*, syphilis), a drain on the system (pregnancy, lactation), a cachectic condition, or most commonly an imperfect reduction or inefficient immobilization of the fragments, the fibrous callus which unites the fragments fails to ossify after a sufficient length of time has elapsed, the bone formation should be stimulated by attention to the patient's general condition and such measures as will produce local irritation. Among the local measures the most successful have been the production of congestion by occasionally constricting the limb above the point of fracture for a sufficient time to cause decided venous congestion, the **injection of** from 5 to 10 c.c. (1¼ to 2½ drams) of the **patient's blood** removed from a vein into and about the fractured area (Bier), the injection of a few drops of a 10 per cent. solution of the **chloride of zinc** into the callus, the use of **electricity** with one needle in the callus and the other on the surface of the limb, or the wearing of a splint loose enough to allow a slight amount of motion at the point of fracture. These failing, the only alternative is to cut down on the fracture, to cut away the callus, and suture the bones into place with catgut. If a gap remains it may be filled in by a **bone graft** removed from the tibia or a piece of the patient's rib; either placed in a groove cut in the bone-ends or placed as an intramedullary graft after boring out the bone-ends down to the normal medulla. In either case the graft must be in contact with living bone at each end. A gap in the tibia may be done away with by removing a section of the fibula. The use of wire is contraindicated here as elsewhere, except for temporary service. One need scarcely add that if the defective union is due to the general condition of the patient, no amount of operating will make the fracture unite so long as that condition persists.

In the treatment of true non-union of bone, that is, cases in which lime salts are not properly thrown down, there are two indications. The first is to increase the quantity of lime salts contained in the blood; the second, to induce a larger quantity of blood to flow through the affected bones. The first indication is met by the administration of **calcium salts,** usually in the form of the **hypophosphites. Thyroid gland** has also been recommended, though its action is uncertain. The diet and personal hygiene of the patient should be carefully regulated. The second indication must be carried out by local measures. Any foreign substance imbedded in tissue induces a hyperemia. If, then, we insert a sterile foreign body that can be gradually absorbed, we have the ideal condition of bringing more blood to the region, and, at the same time, attracting leucocytes for its absorption, and so accomplishing the gradual disappearance of the foreign body after union of the bone has occurred. For this purpose Dr. Charles Mayo inserts a sterile ivory pin into the medulla of the bone. **Bier's hyperemia** method is useful in conjunction with the foregoing measures. Horsley (Jour. Amer. Med. Assoc., Feb. 3, 1912).

Nearthrosis, a very rare condition, in which the bone-ends are separated by a joint-cavity, demands operative interference.

Faulty or angular union may be remedied by **osteotomy.**

SPECIAL FRACTURES.

FRACTURES OF THE SKULL.

— Varieties. — Instead of dividing these fractures, according to their location, into fractures of the vault and of the base, it is more intelligible to speak of

1. *Circumscribed fractures,* with little injury to the brain.
2. *Fissured fractures,* usually associated with serious brain lesions.
3. *Intermediate and irregular fractures*—the intermediate fractures that combine some of the features of each of the above varieties.

Circumscribed fractures being usually caused by a sharp blow from some pointed object, the skull is crushed locally, without any great injury to the underlying parts. In typical cases, after the shock of the blow has passed off there is no further danger or inconvenience, except the danger of infection, for almost all fractures of the skull are compound. Sometimes the outer table alone, again (but rarely) the inner table alone, and usually the whole thickness of the skull is depressed. Yet there may be no depression, the skull being simply split (locally) at the point of fracture.

The *diagnosis* may be easily made by inspection and palpation. If, however, the fracture is not compound, a ridge of clotted blood may feel like the overhanging edge of the uninjured bone over a depression; but in the case of the clot the finger goes up one side of the ridge as well as down the other, and does not simply slide over the ridge, and firm pressure will indent the clot, but not the skull.

Fissured Fractures.—These fractures are caused by the "bending" or "bursting" of the skull under pressure applied broadly. They are the "indirect" fractures of the skull, just as the circumscribed fractures are "direct." Consequently fissured fractures are much more common in the base, and circumscribed fractures more common in the vault. The bursting force may make itself felt in a radial direction or in a direction at right angles to this, and the fissures are therefore usually dispersed in one of these two directions, although the irregular thickness and elasticity of the skull, especially its base, is liable to impart to the fissure a zigzag course. The fissure may occur only at some point quite distant from the point of impact and is there often termed a *contrecoup,* a misleading term, for there is no *contrecoup.* On the other hand, the fissure may be so extensive as to allow the two halves of the skull to be freely movable upon each other. Since the cause of those fractures is generally a blunt instrument, they are less often compounded than the circumscribed fractures.

These fissures being due to a bursting of the skull on account of a sudden change of shape of the whole globe, it is readily understood that the associated lacerations of and hemorrhage into the contained structures are likely to be very extensive and to prove rapidly fatal, not in any sense on account of the fracture, but on account of the trauma that caused the fracture.

DIAGNOSIS. — Fissures in the vault are often compounded and thus readily diagnosed. Care must be taken not to mistake a lacerated aponeurosis for a fissure of the skull. In fissures of the base, however, the diagnosis can rarely be made except by inference. As these fissures often involve the petrous portion of the temporal bone, rupturing the tympanum, hemorrhage from the ear, mouth, or nose is a fairly accurate diagnostic sign of fracture of the base. The diagnosis is, however, of very little importance.

Intermediate and Irregular Fractures.—Most fractures of the skull are, in a sense, intermediate between the two great divisions of circumscribed and fissured fractures, for with every sharp blow there is seen to be some compression of the whole globe, and even the bluntest force, if applied with sufficient momentum, will cause a local crushing. But an understanding of the two great classes will elucidate all such cases. Exceptionally the brain is compressed by the blood effused beneath a circumscribed fracture, and its evacuation is followed by immediate relief of symptoms; but, we repeat, such cases are exceptional.

Punctures.—Those which cause a local fracture are very liable to produce a local brain lesion and to lead to infection; hence they present special therapeutic indications.

Ring fractures around the foramen magnum are caused by a sudden blow upon the buttocks which forces the spine up into the skull, carrying a ring of the basilar portion of the occipital bone along with it.

PATHOLOGY.—A piece of depressed bone may lacerate both dura and pia and even the brain. In so doing it may tear the great sinuses or the middle meningeal artery. If the fracture involves the inner ear, the hearing may be permanently lost. Various nerves and vessels and the cord itself may be torn at their points of exit from the skull. Any amount of brain laceration may accompany the fracture.

Process of Repair.—Most of the membrane formation is done by the diploë, the osteopoietic faculties of the pericranium and dura being very slight. Consequently there is very rarely any superabundant callus, and consequently, too, if a piece of skull is removed it will be replaced only by fibrous tissue, and not by bone.

PROGNOSIS.—The gravity of the prognosis depends on two things, either of which may exist without any fracture at all, namely: the damage to the brain and its adnexa, and infection. The importance of depressions of small areas of the vault has been unduly magnified. Stimson strongly advises against meddling with simple depressed fractures unless focal symptoms present themselves. It is certainly absurd to suppose that the depression of a square inch of bone to the depth of half an inch or so could cause the severe and lasting shock that is so often attributed to such an injury, nor should the elevation of such a splinter be expected to relieve these grave disorders.

TREATMENT.—**Simple Fractures.**—Attend to the general condition of the patient and leave the fracture alone unless focal symptoms present themselves as the result of a depression or a hemorrhage from the middle meningeal artery. In such cases operate to elevate the depression or to stop the hemorrhage. Many surgeons hold that all depressed fractures should be elevated at once. As the choice lies between the problematical danger from the existing depression and the real danger from possible infection, the question cannot be said to be definitely settled.

Compound Fractures.—Operate immediately for the purpose of cleansing the wound. Fill the wound itself with gauze, then shave and cleanse the whole scalp, or at least half of it. Next enlarge the skin-wound if necessary in order to catch all bleeding points and to expose the laceration of the soft parts. If there is any depressed bone it can usually be elevated by prying up the most elevated corner and extracting this piece by gentle manipulation with the forceps, after which the rest will follow easily. Occasionally the chisel or trephine may be necessary; but in all compound fractures the bone must be elevated for the purpose of assuring the asepsis of the subjacent tissues. Having elevated and removed the splinters the whole wound is copiously irrigated with "normal" salt solution. If any intracranial hemorrhage persists, the wound must be left packed with sterile or iodoform gauze for forty-eight hours, after which it may be closed. If there is no bleeding the dura is sutured if torn, and the pericranium, aponeurosis, and skin sutured in layers, the first three with catgut, the last with silk. An aluminium, silver, or celluloid plate or a sheet of goldfoil or rubber tissue may be interposed in the gap left by the removal of fragments of bone in order to strengthen the scar.

The writer considers **decompression** as the only correct treatment for basal fractures of the skull, as indicated by the experimental results of Hill, Cushing and Krause. Heretofore, the treatment had been irregular and the mortality 64 per cent. up to within the last five years. He reports a case treated by decompression, with remarkably good effects closely following. There was complete paralysis of the lower right face, right half of the tongue, the right arm and leg. The breathing was stertorous, close to 44. There was high blood-pressure, pupillary dilatation and profound unconsciousness. A large osteoplastic flap was turned down, the dura found to be very tense. When nicked, the cerebrospinal fluid came out in a jet. The patient's pulse immediately rose to 70, and twelve hours afterward he could move the paralyzed foot slightly.

At the end of a week he had regained the use of his tongue, arm and leg, but the facial paralysis still persisted at the time of his discharge, though he was otherwise completely recovered. R. L. Payne, Jr. (Jour. Amer. Med. Assoc., Feb. 17, 1912).

If a fissure of the skull appears in the wound, it should be thoroughly cleansed as far as infection may have traveled, the wound being slightly enlarged and the edge of the fissure chiseled away for this purpose, if necessary. There is no object in endeavoring to find the limits of the fissure, which may extend halfway around the skull or even farther. If from the force of the blow a depression of the inner table seems possible, that is no indication for increasing the patient's risks of brain infection by trephining. Such depressions are extremely rare, and unless they give rise to focal symptoms they are innocuous.

Experiences with 530 cases of fracture of the skull at the Obuchow hospital in St. Petersburg. In 18 cases the broken-off pieces of the skull were reimplanted and the results confirm the superior advantages of this measure; 14 of the patients made a smooth recovery. In the 166 cases of fracture of the base of the skull the mortality was 61 per cent.; treatment here can be only conservative and symptomatic. The prognosis is much better with fracture of the convexity of the skull; the mortality was only 25 per cent. in the 206 cases of this kind in which an operation was attempted among the total 364. In 14 of the cases local anesthesia sufficed. The mortality in the fatal cases was almost exclusively the result of the injury to the dura from the accident. When the brain is injured too, the prognosis is still graver; the mortality was 56 per cent. in his 56 cases of this kind, nearly all the patients succumbing to suppurative meningitis. Schaack (Jour. Amer. Med. Assoc. from Archiv f. klin. Chir., Bd. xcvii, Nu. 3, 1912).

Punctured wounds should always be opened up, the punctured part of the skull being entirely removed by the trephine and the whole wound then irrigated and drained. Bullets located near the surface may be removed at once; if deeper and not to be touched by gentle probing, they had best be left alone, as their presence does not materially influence the prognosis. If they give rise to symptoms later, they may be located by the X-rays and their removal attempted with a greater prospect of success. Infection from the air-passages in fractures of the base cannot very well be guarded against. It is futile to render the middle ear aseptic when germs may constantly reach it through the Eustachian tube.

FRACTURE OF THE VERTEBRÆ.—The importance of fractures of the vertebræ, like those of the skull, is dependent almost entirely on the amount of damage done to the inclosed nervous tissues; on this the symptoms, prognosis, and treatment depend.

Symptoms.—The symptoms are mainly those of an injury to the spinal cord. If the displacement is such as to compress or tear the cord, paraplegia results, with loss of control over the vesical and anal sphincters, and in the male priapism usually occurs. Locally there is tenderness and pain, increased by motion, ecchymosis, and deformity, and crepitus in some cases.

Diagnosis.—Except the deformity and crepitus, any or all of the above symptoms may be caused by injury to or disease of the cord without any fracture of the spine. Hence the diagnosis is generally obscure; but no manipulation should be undertaken for the purpose of elucidating it, for fear of precipitating a fatal issue. Fracture and dislocation are usually associated, and their differentiation is of no clinical importance.

In estimating the location of the injury, it must be remembered that the pressure symptoms may be due as well to hemorrhage or inflammation as to the displaced bone, and also that it may take twenty-four to forty-eight hours for the paralytic symptoms to appear at their distinctive level. Hence the local symptoms of pain, tenderness, and deformity are much better guides to the level of the lesion than the paralytic and anesthetic symptoms.

> The sensory symptoms offer the most reliable information as to when to operate. When, for instance, the anesthesia presents a line of sharp segmental limitation and does not improve within twenty-four hours, operation is advisable, as intradural hemorrhage is probably present. If, on the other hand, the anesthesia is irregular, or if it improves early, operation should be deferred, as the cord is probably not greatly injured. Operation several months after the injury, where the symptoms had been severe and had not improved, were usually futile. The operations on the spinal column are not in themselves particularly dangerous if done by skillful and experienced surgeons, and offer the best results in properly selected cases. E. D. Fisher (Trans. Amer. Med. Assoc.; N. Y. Med. Jour., June 8, 1912).

Etiology. — Indirect violence, by causing an excessive bending of the spine, is the common cause of fracture. Such violence may be applied by a fall of the subject himself or by some heavy body falling upon him. Less frequently muscular violence produces a fracture of the spine, the usual location of such fractures being the cervical region and the usual cause a sudden jerking backward of the head: as to avoid striking the bottom when diving in shallow water.

Pathology.—The crushing force which causes the fracture is very likely to cause a simultaneous dislocation.

The bodies of the vertebræ are the parts most affected, except in the cervical region, where the transverse and articular processes are more frequently injured. Direct violence occasionally tears away the spinous process. There is no regularity about the fractures, however, every conceivable variety having been observed. The upper fragment is usually displaced forward on the lower one and the cord is compressed, rarely torn across, between the two. Subdural hemorrhage or secondary meningitis may give rise to still further compression. The nerves that make their exit at that particular segment are usually torn, as are the attached muscles and ligaments.

Prognosis.—*Fractures of the Lower Three Lumbar Vertebræ.*—In fractures of this region only the cauda equina is liable to compression, and its individual components can usually slip aside from any obtunding fragment, and thus there will be no pressure symptoms. Under appropriate treatment the bones unite and the patient may recover entirely or with a weak back, or with paralysis or pain from pressure in some of the nerves.

Fractures Above the Second Lumbar.—The prognosis as regards life and death varies with the amount of damage done to the cord. If the cord is permanently damaged, the patient may continue to live as long as two months, only to die finally of exhaustion or of septic infection from bed-sores or catheterization. Death may be instantaneous from shock or from involvement of the phrenic nerve in the laceration. In fractures high up in the cervical region, even of the atlas and axis, death is not always instantaneous, but the least movement or jolt may be enough to bring fatal pressure to bear on the cord.

> The writer has had 2 cases of fracture of the cervical vertebræ without spinal-cord symptoms, and emphasizes the importance of Roentgenoscopic control and the necessity for shielding such patients from hard work, possibly for a year, as otherwise there may be serious damage from resumption of work before consolidation is complete. Boeckel has recently compiled 95 cases of the kind, including 14 previously unpublished. Isolated fracture of the body of the vertebra occurs most frequently and a sliver of bone may be felt through the mouth in the pharynx. Extravasation of blood may compress the cord for a time, causing paralysis, but as the blood is absorbed the paralysis retrogresses. Sonnenburg (Berl. klin. Woch., Feb. 19, 1912).

Treatment.—In all manipulations the greatest care must be exercised to avoid the production of farther displacement. The patient must be kept upon a water-bed, catheterization must be conducted with every precaution, and the bladder irrigated daily with a saturated watery solution of **boric acid**, or, if cystitis supervenes, with a 1:4000 solution of **nitrate of silver.** Pressure must be taken off spots where bed-sores threaten, and, if they occur, they must be kept clean and dry by antiseptic powders. Nor must the patient's general vitality be neglected. As long as there is any hope of recovery **electricity** and **massage** to the paralyzed muscles are advantageous, and the strictest cleanliness must be insisted upon. The curative measures are mechanical and operative.

Mechanical Treatment.—This originally consisted in traction upon the head and feet by two assistants while the surgeon endeavored to reduce the fracture by direct manipulation. More recently suspension and the application of a plaster jacket, as for Pott's disease, has afforded some good results, and a similar treatment is that of Dr. Woodbury's, who applied the jacket to a child upon whom traction was being made while it lay face down upon a hammock of cheese-cloth. Dr. Stimson advocates suspension along a plank, the plaster being applied while pressure is maintained on the protuberance.

Operation.—The so-called **laminectomy** is done through a long vertical incision with its center over the fractured vertebræ. The bone is bared and the spinous processes of three or four of the vertebræ removed. Then with rongeur forceps the laminæ are divided on either side as close as possible to the transverse processes. The dura is then exposed and, if distended with pus or blood, it is incised and drained. Otherwise it is gently retracted and the bodies of the vertebræ are palpated.

Any unevenness in the vertebræ is to be removed, the straightening of the whole column attempted, and the wound closed without drainage, unless hemorrhage or suppuration demand it.

The results of operation have been so unsatisfactory even at the hands of its most earnest advocates, and the effect of traction and the plaster jacket so manifestly advantageous, that the mechanical method is the treatment of election even though operation has occasionally disclosed and remedied pathological conditions upon which no manipulation could have exercised a beneficial influence.

FRACTURE OF THE NASAL BONES.—The nasal bones, cartilages, and septum may all be fractured. Such fractures may be followed by tedious suppuration, facial emphysema, plugging of the lachrymal canal, and, as the displacement is always backward, some subsequent deformity is inevitable, unless they are replaced.

Diagnosis. — By endeavoring to move the upper and lower parts of the nose laterally upon each other, false motion and crepitus will thus be elicited.

Treatment.—This must be begun promptly, for osseous union has been known to occur by the tenth day. By means of a director passed within the nostrils the bones are replaced. The only retentive apparatus of any value is a long pin passed directly through the nose and resting on either cheek, the nose being covered with a piece of adhesive plaster. As a general rule, however, there is no tendency to reproduction of the deformity, and, even if such a tendency does exist, frequent reposition will appeal to the patient rather than the transfixion treatment. In old unreduced fractures an artificial bridge of aluminium, celluloid, or gutta-percha may be introduced and is well borne.

FRACTURE OF THE MALAR AND SUPERIOR MAXILLARY BONES.—Fractures of these bones, beyond the subsequent liability to suppuration and emphysema, are of no particular importance. If a fracture of the zygoma threatens a serious deformity, it may be remedied by inserting a sharp hook under the process and so elevating it. Fractures of the alveolar process of the jaw with displacement should be treated by wiring the teeth, or by an interdental splint (*vide infra*).

To replace a depressed, fractured malar bone, the writer uses the ordinary cow-horn forceps of the dentist, which, in addition to sure control, has the advantage of leaving no scars, is quickly used, and does not require any opening in the mouth. The skin over the bone is suitably prepared; one point of the forceps is placed over the orbital ridge and the other just under the margin of the body of the bone at its outer side; a little pressure penetrates the skin and the points grasp the depressed bone with any degree of firmness advisable. Now the more or less impacted bone is disengaged from its bed, elevated to its proper place, and the forceps removed at once. No dressing is necessary, as the holes in the skin are mere pricks. J. G. R. Manwaring (Jour. Amer. Med. Assoc., Jan. 25, 1913).

FRACTURES OF THE LOWER JAW.—The body, the ramus, the condyle, or the coronoid process may be fractured. Fractures of the body are, by far, the most common. They are almost always compound and occur usually in the middle line or else are double, one on each side. Unilateral fractures are comparatively infrequent. The displacement is usually vertical and from before backward, as well. It may be appreciated by the finger inside the mouth. In fractures of the ramus there is little or no displacement. In those of the condyle that process is usually drawn forward on to the eminentia articularis, the lower fragment slipping up into the glenoid cavity and so causing the chin to deviate to that side.

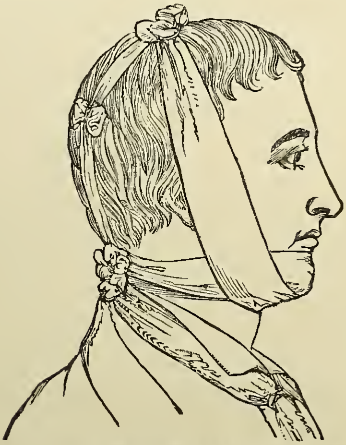


Fig. 1.—Four-tailed bandage for fracture of lower jaw. (*Stimson.*)

The diagnosis is easy except in fracture of the ramus, where local tenderness and pain on closing the jaws may be the only symptoms.

Treatment.—A mild antiseptic wash should be employed frequently to lessen the danger of infection and to clear the mouth of the foul and acid discharge from the wound. Under such treatment with efficient immobilization the wound may be expected to heal kindly, though occasionally it is impossible to prevent suppuration and necrosis.

IMMOBILIZATION.—Though reduction is easy, the deformity tends to reproduce itself, to overcome which tendency a great number of mechanical devices have been introduced. The principle employed are external pressure, exemplified by the four-tailed bandage (Fig. 1), wiring of the bone or teeth (several on either side lest they pull out), and the interdental splint. This is a piece of gutta-percha or vulcanized rubber molded to fit between the upper and lower teeth, and of such width as to hold the jaws slightly separated so that fluids may be introduced through a hole bored in its center. This is applied and the jaw bound firmly by a four-tailed bandage. The first two methods may prove satisfactory; but the dental splint, though more complicated, is quite sure to give satisfaction if it is made by an expert dentist.

The molded lead splint introduced by Matas is most satisfactory and may be used until an interdental splint can be made.

An experience with 76 cases of fracture of the lower jaw showed the writer that it is typically a fracture occurring at a place where the resistance is weak, due to anatomical, physiological, or pathological characteristics. The active agent in the displacement of the fragments is muscular contraction, the force of the trauma and the course of the fracture line being determining factors. Suture of the bone is indicated only in toothless jaws. Splints serve best in jaws which have teeth and are the least annoying to the patient. The splints should fit firmly and should be made of sterilizable material. Egger (Beiträge z. klin. Chir., Bd. lxxvii, Hft. 1, 1912).

FRACTURE OF THE HYOID BONE, THE LARYNX, AND TRACHEA.—These rare fractures are usually caused by direct violence, as in strangulation. They may be recognized by direct palpation. They endanger life by obstructing respiration. If the symptoms are urgent, tracheotomy should precede attempts at reduction.

FRACTURE OF THE STERNUM.—This accident is very rare. It is usually caused by the strain of bending forward or backward. The symptoms and treatment are those of dislocation (*q.v.*).

FRACTURES OF THE RIBS.—These are frequent, though often multiple, and occur usually between the fifth and ninth. The upper and lower two ribs are almost never fractured. In single fractures there is, as a rule, no displacement; but multiple fractures may give an angular displacement, or, if sufficiently extensive, a caving in of the whole side of the chest. The fracture may be located by a localized point of tenderness (and crepitus), which may be elicited by pressure on the shaft of bone at a distance from the fracture. Crepitus may also sometimes be elicited by deep inspiration, which is painful. If the lung is pierced there may be cellular emphysema, hemoptysis, and later a pneumothorax.

Treatment.—Displacement having been corrected, the bone is immobilized by strapping the chest with adhesive plaster. During expiration a strip of plaster two inches broad is applied, beginning over the sternum and following the curve of the ribs over the point of fracture, and around to the opposite axilla. If several ribs are broken they are covered from above downward by similar strips overlapping.

It is necessary to watch fractures of the ribs carefully for a couple of days to note the onset of pulmonary complications. Localized pneumonitis sometimes occurs. In strapping the chest for fractured ribs, the straps should pass well beyond the median line. They should be applied during full expiration. One or two straps passed over the shoulder help much to secure immobilization. Fuld (Internat. Jour. of Surg., June, 1912).

FRACTURE OF THE COSTAL CARTILAGES.— See DISLOCATIONS.

FRACTURES OF THE CLAVICLE.—They are very frequent in children, being caused by a fall upon the arm which in an adult would be more likely to dislocate the shoulder. They occur usually in the middle third of the bone, are not infrequently incomplete, but very rarely compound.

Fractures of the middle third are transverse or oblique, from above downward and inward. The shoulder, losing its anterior support, drops downward, inward, and forward; the posterior border of the scapula is raised outward and its lower angle rotated slightly upward and backward. If the fracture is oblique the outer fragment slips below and behind the inner one, whose edge is prominent under the skin. Transverse fracture may give rise to angular deformity, the angle pointing upward and backward. If the fracture is comminuted the small fragments are markedly displaced; if it is bilateral the weight of the two shoulders on the chest may cause urgent dyspnea (relieved by dorsal decubitus). Injuries to the great vessels, nerves, and lungs are rare complications. The arm can be moved forward or backward, but cannot be abducted on account of the pain rather than the muscular disability.

In fractures of the outer third the line of fracture is usually tranverse and the displacement angular, with the apex backward. Disability and deformity are not great.

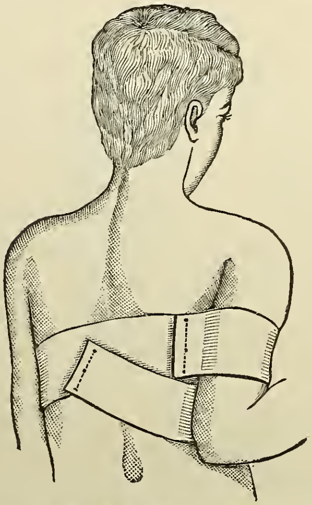


Fig. 2.—Sayre's adhesive-plaster dressing for fracture of clavicle. First piece. (*Stimson.*)

In fracture of the inner third the outer fragment passes below the inner one or is accompanied by it, producing angular deformity.

Prognosis.—Union is almost certain to take place at the end of four weeks whether the fracture is immobilized or not. Some persistent displacement is the rule, especially in adults.

Treatment.—Reduction is effected by pushing the shoulder upward, outward, and backward. Manipulation of the arm or simple dorsal decubitus will effect this. To maintain perfect reduction dorsal decubitus with the head slightly raised and the forearm resting across the chest is usually essential. In the green-stick fractures of children a simple sling may be sufficient, and the same dressing may be applied to all patients who are impatient of restraint in the more complicated dressings and are willing to accept the subsequent deformity.

In other cases Sayre's or Velpeau's dressings will produce an esthetically satisfactory result.

Sayre's dressing (Figs. 2 and 3) requires two strips of adhesive plaster, each three inches broad and long enough to reach one and a half times around the body. The end of one strip is fixed loosely about the arm on the injured side just below the axilla. It is then carried around the back and across the chest in such a way as to hold the elbow a little behind the axillary line. The other strap is then carried from the uninjured shoulder across the back and the point of the elbow and back to the point of starting, carrying the elbow forward, upward, and inward. Thus the shoulder is carried upward, outward, and backward. The axilla and the whole inner surface of the arm and forearm should be well padded with cotton or wool, and the bony points of the elbow should be protected in like manner. The band had best be left uncovered and the whole dressing supported by a few turns of a roller bandage.

Dressing of heavy moleskin plaster to avoid skin irritation of zinc-oxide plaster and prevent looseness of dressing requiring reapplication: Warm a piece of moleskin 4 or 5 inches wide by 18 long, loop it about humerus high up in axilla, join its ends, and insert eyelets in them for lacing. Place a second strip around the healthy side of body and adapt its posterior end for lacing with humeral loop, thus drawing shoulder of injured side back. Next place a piece of moleskin 7 x 10 inches over healthy shoulder as a cap, and insert eyelets in the free ends anteriorly and posteriorly. Pass a long strip 3 inches wide around the forearm of the injured side close to elbow, and connect the ends in front of and behind the body by laces with shoulder cap on healthy side, thus providing for elevation of the injured shoulder. By tightening one lacing more than the other, the elbow may be brought forward or back as desired. Wait till the adhesive plaster is well secured to the skin before tightening the laces. Collins (Annals of Surgery, Jan., 1912).

Velpeau's dressing, as shown in Fig. 4, holds the elbow pressed against the front of the chest. It is made with a roller bandage. Padding should be applied as noted above.

Moore's ingenious combination of a posterior figure-of-8 bandage to both shoulders and one elbow with a sling (Figs. 5 and 6) is effective, but uncomfortable, and unless carefully padded is likely to interefere with the circulation of the arms.

Fracture of the outer third is best immobilized by Stimson's dressing for dislocation of the outer end of the clavicle (*q.v.*).

To avoid deformity displaced comminuted fragments may be removed through a small incision.

FRACTURES OF THE SCAPULA are divided into fractures of the body of the lower angle, of the spine, of the acromion, of the coracoid process, of the surgical neck, and of the glenoid fossa.

Fractures of the body and inferior angle may be partial or complete, simple or comminuted. When the angle is torn away it is drawn forward by the attached muscles and cannot be replaced. In fractures of the body displacement is usually confined to overlapping of the fragments. The diagnosis is made in either case by palpation, and the sole treatment is immobilization by plaster strapping, as for fractures of the ribs, and support of the arm by a sling. The only complication to be feared is suppuration in the deeper planes, which may follow even a simple fracture if the contusion has been severe.

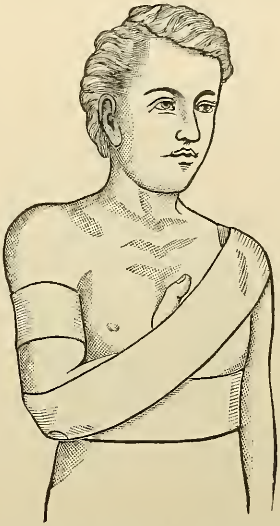


Fig. 3.—Same as Fig. 2. Second piece. (*Stimson.*)

Fracture of the acromion may be caused by external violence acting directly or through the humerus, or else by contraction of the deltoid. The fracture is usually beyond the attachment of the clavicle. Non-union of the epiphysis may occur. Bony union can rarely be obtained, but no disability follows fibrous union.

TREATMENT. — Velpeau's dressing (Fig. 4).

Fracture of the coracoid process

may be caused by external violence or muscular action and is often complicated by other injuries. Abnormal mobility, with or without crepitus, may be obtained by pressure on the tip of the process. Fibrous union without disability is the rule.

Treatment.—Treatment is by immobilization of the arm in slight hyperextension.

Fracture of the Surgical Neck.—Either the whole of the glenoid fossa or only a part of it is torn off with the long head of the triceps attached to the fragment. The support of the triceps being lost, the whole shoulder sinks downward and the displacement resembles very closely a subcoracoid dislocation. The arm, however, is not abducted nor is there any characteristic restriction of motion; a lump may be felt in the axilla, and the deformity may be reduced (with crepitus) by lifting the arm, but immediately recurs.

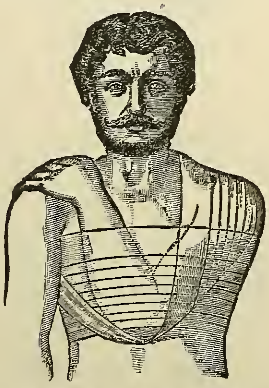


Fig. 4.—Velpeau's dressing for fracture of clavicle. (*Stimson.*)

Treatment.—The treatment is as for dislocation of the clavicle; bony union may be expected.

Fracture of the Glenoid Fossa.—The rim is often broken, with dislocations of the shoulder-joint. Stellate fractures have been found *post mortem.*

FRACTURES OF THE HUMERUS.—These may be conveniently grouped into fractures of the *upper extremity,* of the head, anatomical neck, through the tuberosities, of either tuberosity, of the surgical neck; and separation of the epiphysis, of the *shaft,* and of *the lower extremity;* supracondyloid, intracondyloid, of either condyle, or epicondyle; and separation of the epiphysis.

Fracture of the Head.—This is very rare, excepting the splitting that may accompany dislocation, and cannot be recognized clinically.

Fractures of the Anatomical Neck and Through the Tuberosities.—These present the same clinical features and can rarely be differentiated before death; indeed, the line of fracture is likely to be so irregular as to be partly through the neck and partly through one or other tuberosity. These lower fractures are certainly more frequent than simple fractures of the anatomical neck. Most cases occur in connection with anterior dislocation. There may or may not be impaction. If the head is dislocated forward it may be felt, and its independent mobility recognized when the shaft of the bone is rotated. If the head is not dislocated, pain in upward pressure on the elbow may be the only symptom.

Treatment.—If the head is not dislocated, treatment is by immobilization with slight traction. If it is dislocated, alternatives present themselves: The surgeon may maintain the two fragments in apposition, hoping to obtain union, and then at the end of five weeks to attempt reduction by manipulation, or, this failing, by operation. On the other hand, he may, and this seems the better plan, attempt reduction at once. If his manipulative efforts do not succeed, he may attempt operative reduction, laying bare the head, boring a hole in it, and then reducing it by means of a stout right-angled hook (McBurney) inserted into this hole. Failing in this, he may exsect the head. In any case the area should be immobilized for five weeks. The theory that the head subsequently atrophies has no very good foundation in fact. On the contrary, very good functional results are obtainable.

Fractures of the tuberosities occur in connection with dislocation of the shoulder forward (greater tuberosity) or upward (lesser tuberosity). As the fracture is often incomplete, bony union without much deformity is the usual result.

Separation of the epiphysis may occur at any time during the first two decades of life. The most common mechanism of its production is probably hyperabduction in the efforts to pull down the arm during labor. The line of separation runs just below the tuberosities and the usual displacement is of the lower fragment more or less completely to the inner side and in front of the upper one, which is tilted outward. The edge of the lower fragment may be felt or even seen close under the skin in front. Crepitus is slight, owing to the cartilaginous nature of the edges. Reduction is by manipulation or by forced abduction, which brings the lower fragment in line with the upper one. Union may be irregular if the periosteum slips between the fragments. Immobilization must be maintained for five weeks. Persistent displacement or premature ossification of the epiphysial cartilage may arrest the growth of the limb.

Fracture of the surgical neck is by far the most common of the fractures of the upper extremity of the humerus. Under this head are classed all fractures between the line of the epiphysial junctures and the insertion of the pectoralis and teres major. They are caused by direct violence or a fall upon the elbow. The displacement is usually slight, but the lower fragment may be drawn up and to the inner side of the upper one, which is then held in abduction. The diagnosis is made by eliciting abnormal mobility and crepitus when the tuberosities of the humerus are firmly grasped and the arm gently rotated. In impacted fractures there is a tender spot just below the tuberosities and the arm is usually held in slight abduction.

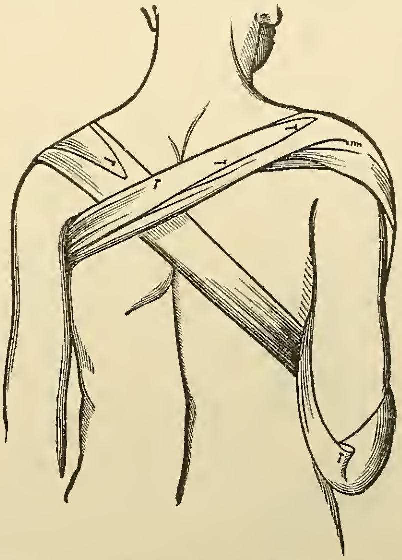


Fig. 5.—Moore's dressing for fractured clavicle. (*Stimson.*)

In a fracture dislocation at the shoulder-joint the fracture usually occurs after the dislocation, and is caused by ill-advised and unskillful efforts at reduction; for operations under proper conditions and for proper purposes the shoulder-joint exhibits great tolerance; the shoulder-joint possesses a remarkable ability to adjust itself to a great amount of damage and injury, eventually recovering its functions. Bissell (Med. Rec., April 6, 1912).

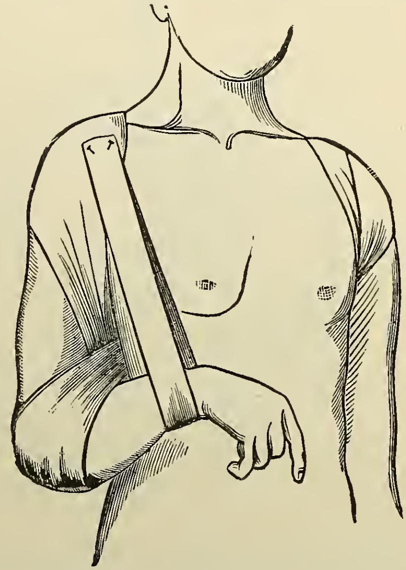


Fig. 6.—Moore's dressing for fractured clavicle. (*Stimson.*)

Treatment.—If there is much overriding, reduction can only be effected by traction in extreme abduction. If the fragments are impacted in fair position, or if there is no displacement, as is often the case, any immobilizing dressing will be sufficient. Usually, though, there is some tendency to shortening to be overcome by traction and often some abduction in the upper fragment that cannot be overcome. To meet these indications various splints have been devised. For abduction of the upper fragment the best treatment is generally to keep the patient in bed and traction by weight and pully (see Fractures of the Thigh) on the arm held in partial abduction by being bandaged on a triangular pad or a bent metal band fitted into the axilla. After two weeks sufficiently firm union will probably have taken place for the arm to be abducted. In this position it is maintained for three or four weeks longer, by a plaster mold or circular splint of which the uuper edge is molded well over the shoulder to immobilize the joint, and which is made light over the forearm (the elbow being bent to a right angle) and heavy over the arm. The whole is bound lightly to the chest and the wrist above supported by a sling, in order that the weight of the arm may tend to prevent shortening. Any shortening that may occur will be indicated by a rising of the shoulder-cap and must be compensated by weights attached to the elbow. During all this time frequent exercise of the wrist and fingers must be insisted upon.

A variation of the above line of treatment should be effective in any case. Ambulatory treatment with the arm in abduction is possible, but irksome.

A simultaneous dislocation of the head is treated as above indicated.

Fractures of the Shaft.—These are caused by external violence or by muscular action. All varieties of fractures and displacements are seen here. The vessels or nerves may be injured, notably the musculospiral, which may be torn across, pressed upon by the callus, or caught between the fragments. Union is more likely to fail in this than in any other bone: a fact that has been explained by deficiency of immobilization, for, since the hand is supported by a sling every motion of the head and neck imparts a slight movement to the fragments.

The treatment is along the same lines as that of the surgical neck. Shortening must be carefully watched for and prevented.

Supracondylar Fracture.—The line of fracture passes through the lower part of the humerus, just above the condyles. The joint is usually not involved, but may be opened by an additional intercondylar fracture or fracture of the olecranon. The line of fracture is usually from behind downward and forward, and consequently the lower fragment is displaced upward and backward. The sharp point of the upper fragment may pierce the skin in front; more rarely the fracture is compound from behind by the lower one. If the swelling is not too great the displacement can be seen as well as felt, and false motion and crepitus elicited by moving the condyles on the shaft. Dislocation is ruled out by the normal relation of the olecranon and epicondyles, as compared with the other arm, and intercondyloid fracture by the absence of its typical symptoms (*q.v.*).

> The writer states that transverse ecchymosis at the bend of the elbow in fracture of the lower extremity of the humerus is found so constantly in association with fracture of the lower portion of the humerus with forward displacement of the upper fragment as to be of assistance in the diagnosis of this variety of fracture from backward dislocation at the elbow. If the case is seen early, the ecchymosis is very distinct and exactly transverse, as though produced by a blow with a thin, heavy instrument. Later, it becomes diffused and is less distinct. E. Kirmisson (Bull. de l'Acad. de Méd., April 23, 1912).

TREATMENT.—Same as for fractures of the lower part of the shaft: immobilization with the elbow flexed at a right angle and the forearm in semipronation. A sufficient weight, usually five pounds, should be suspended at the elbow to prevent shortening, and the *hand alone* suspended in a sling. Suspension of the whole forearm gives rise to angular deformity with adduction of the forearm.

Treatment by extension may be advantageously combined with suspension of the limb in a vertical position for the first fortnight of treatment of a compound fracture; but as this position tends to tilt back the lower fragment it should never be employed except as just mentioned and then only for the advantages of elevation in the healing of the wound.

> Features which are peculiar to fracture of the humerus in children. In the writer's 78 cases of fracture just above the condyle, the final outcome was excellent in all but 2 cases. In 42 cases of fracture of the external condyle, 6 of the children were left with more or less deformity, although the outcome as regards functioning was not bad.
>
> Excepting those cases in which dislocation of the humerus occurs and is overlooked, the prognosis of fracture of the epitrochlea is good. In 3 of his 21 cases of fracture of the epitrochlea an operation was necessary, but the outcome was equally favorable in all but 2 of the 12 cases with dislocation. A. Treves (Arch. de méd. des enfants, Oct., 1912).
>
> The writer practised a circular resection and suture of the axillary artery for transverse laceration by fracture dislocation of the anatomical neck of the humerus at the site of the laceration and re-established its continuity. The patient made a good recovery, but has never had a distinct radial pulse, and up to the time of writing has considerable spasticity and some limitation of motion at the shoulder. Buchanan (Surg., Gynec. and Obstet., vol. xv, p. 648, 1912).

Intercondyloid Fracture (T- or Y-fracture).—This differs pathologically from a supracondylar fracture only in the additional line of fracture separating the condyles. The additional force usually required to produce such a fracture is such that the displacements are varied and likely to be marked, and the fracture is often compound and associated with injuries of the adjacent vessels and nerves. In doubtful cases the characteristic symptoms to be sought for are mobility of the condyles upon each other, usually with crepitus, and, in still more obscure cases with no displacement, simple tenderness when the two condyles are pressed against each other.

Treatment.—The treatment is that of supracondylar fracture with additional care in the immobilization of the fragments. Anterior and posterior plaster splints are usually satisfactory. In compound fractures, where the joint is widely laid open, Kocher advises the removal of the external condyle to facilitate drainage and to produce a fairly strong and movable joint. In some cases it may be necessary to remove both condyles with the risk of substituting a flail joint for an ankylosed one. In all compound fractures the fragments should, of course, be retained in place by suture or temporary pegging with a nail or drill.

Fracture of the Epitrochlea, or Internal Epicondyle.—This occurs in connection with dislocation of the elbow or as the result of direct violence. The fragment is left more or less closely attached to the condyle and its mobility may be readily recognized. Paralysis and neuralgia from pressure on the ulnar nerve have been known to follow this fracture. A spontaneous cure may generally be expected.

Treatment.—Direct pressure with immobilization of the forearm in flexion to relax the attached muscles. Two or three weeks' treatment suffices.

Fracture of the External Epicondyle.—This is caused by direct violence and is extremely rare. The mobile fragment is easily recognized and immobilized.

Fracture of the Internal Condyle.—This is caused by indirect violence through forcing upward the condyle with the ulna attached to it. The line of fracture runs from the inner side of the humerus downward and outward to the center of the trochanter or between it and the capitellum. Ligamentous attachment to the ulna usually prevents any marked displacement, and the swelling all about the joints usually obscures such displacement as there is. The forearm is adducted, however, and abnormal adduction and abduction are possible at the elbow. (These movements can only be distinguished from rotation of the humerus when the joint is in full extension: a position but rarely obtainable except under anesthesia.) Independent mobility of the fragment and tenderness on transcondylar pressure should be sought for. Coincident dislocation of the radius backward from the external condyle leaves that part of the humerus prominent anteriorly (see Dislocations). Unless such dislocation is present, the altered relations of the epicondyles and olecranon are likely to be distinguishable through the swelling.

The treatment is by immobilization in the usual semiflexed position. The positions of extreme flexion or extension which have been advocated are inconvenient and present no advantages. If the fragment will not remain in place, it must be cut down upon and fixed by suture. Angular deformity is liable to ensue from suspension of the elbow, as in supracondylar fracture, and may occasionally follow premature ossification of the epiphysial cartilage after fracture of the internal condyle in the adolescent. Excessive formation of callus is likely to impair the functions of the joint, especially in the young.

Fracture of the External Condyle.—The fragment consists of the external condyle, the capitellum, and part of the trochlea. The symptoms are the same, *mutatis mutandis,* as those of fracture of the internal condyle, but the disability is usually less. As more or less rotation of the fragment is liable to occur, the most difficult part of the treatment is reduction, for which an operation may be necessary. Under such circumstances Kocher has exsected the condyle, with good results.

After the reduction has been accomplished there is little difficulty in retaining the fragment in place, and three weeks in a posterior molded splint with the joint at midflexion suffices for a cure. Excessive callus may interfere with the function of the joint.

Separation of the Epiphysis.—This accident is very rare. The epicondyles may or may not remain attached to the upper fragments. The chief symptoms are pain on pressure of the forearm against the arm, abnormal mobility, and cartilaginous crepitus. The treatment is the same as that of supracondylar fracture.

Subepicondylar Fractures.—These usually involve both trochlea and capitellum, very rarely the trochlea alone. If there is no deformity, the fracture may be trusted to heal under immobilization. But if there is persistent displacement the fragment or fragments should be excised. The fluoroscope may be of great assistance in diagnosing obscure lesions about the elbow-joint, but most cases can be diagnosed and treated without its aid.

After-treatment of Fractures about the Elbow.—After the three or four weeks that are necessary to obtain union of the fracture, the elbow will be found quite stiff. If this stiffness is due solely to adhesion and capsular retraction, it may be expected to disappear after some weeks of natural use of the limb. Excessive callus, too, will diminish rapidly, and it is doubtful whether any treatment will hasten its absorption. Forcing of the joint is harmful, as a rule, and if convalescence is too slow elastic traction to increase flexion and a weight on the hand to increase extension may hasten matters a little by supplementing the patient's own efforts. Osteotomy or arthrotomy may be resorted to after several months have elapsed; but the more conservative the treatment, the better will be the results.

FRACTURES OF THE RADIUS AND ULNA.—**Fracture of the Olecranon.**—This may be at the tip or near the base. The mechanism is usually indirect violence combined with the action of the triceps, the olecranon being broken across the trochlea as a stick would be across one's knee. Aponeurotic and periosteal lacerations are usually slight, and consequently there is little or no displacement. The mobility of the fragment is readily recognized.

Treatment.—If the displacement is slight, and is not increased by flexion the elbow may be immobilized midway between full extension and flexion at a right angle. In other cases the elbow must be retained in full extension, and it may even be necessary to pull the olecranon down. The simplest method of traction is by a narrow strip of adhesive plaster running up the side of the forearm over the upper border of the olecranon and down the other side. In cases with separation of the fragments open operation and suture of the torn triceps expansion is indicated. An anterior molded splint gives satisfactory immobilization and permits observation of the displacement. Union is likely to be fibrous, and, in those cases in which this greatly impairs the use of the limb, the fracture may be freshened and sutured.

Fracture of the coronoid process is extremely rare except as a complication of dislocation. As the brachialis anticus and capsule are attached to the bone below the process, its displacement is slight and it unites kindly under immobilization at a right angle (to prevent recurrence of the dislocation).

Fracture of the head and neck of the radius are much more common than was formerly believed. In 29 personal cases (Hitzrot) 19 involved the head and 10 the neck (Annals of Surg., March 12, 1912).

In 15 cases of *fracture of the head* there was but little displacement of the fragments. In 4 cases the fragments were displaced anteriorly.

The disability was rather characteristic in all types. The arm was held in flexion midway between pronation and supination and both the latter movements were impossible. Pain was markedly increased by abducting the arm and pressing over the head of the radius, and especially so, if pronation and supination were attempted in the above position with the above pressure.

Treatment.—In the writer's 15 cases without displacement the arm was supported by a posterior splint, baking begun on or before the third day, and massage before the second baking, *i.e.,* on the fifth day. Movements in flexion and extension were begun as soon as the swelling subsided, usually about the tenth day. Pronation and supination were begun about the fifteenth day. Result: Flexion and extension were complete in all the cases. In 2 cases (chipping off of the radial side of the head) pronation and supination were so slightly altered as to be classed as perfect. In 11 cases pronation and supination were half of that on the normal side. In 2 of the same type as the first 2 mentioned cases, but with the line of fracture beginning well to the ulnar side of the articular surface of the head and extending outward through the head, supination was one-quarter and pronation one-half normal. Both the latter cases have some pain during pronation and supination.

In the 4 cases with displacement of the fragments the X-ray was necessary for diagnosis of the displacement. In 2 the head was broken into three fragments, two of which were displaced anteriorly while one fragment remained in position. In this type the entire head was removed by cutting through the neck about one-half inch below the articular surface of the head and removing the head.

In the remaining 2 cases the head was broken in one place only and the fragment which was radially placed was displaced outward and forward, and in this type the fragment only was removed.

The after-treatment was similar in other respects to that pursued in the fractures without displacement.

Result: The resulting motion was better in those cases in which the head was removed and better in that case in which the most bone was removed (*i.e.*, the neck cut through at the lowest possible level). In the last mentioned case supination was present to seven-eighths the normal and pronation was complete. In the other case of complete removal, supination was two-thirds normal and pronation seven-eighths normal.

In the 2 cases of partial removal of the head supination was one-half normal, pronation two-thirds normal, and pain was present during either movement in 1 of the cases for nearly a year.

The 10 cases of fracture of the neck of the radius were all transverse in type and involved that portion of the shaft about one-half inch below the head. The X-ray was used to confirm the location of the fracture, and in none of the cases was there any marked displacement.

With the arm in the midposition between pronation and supination a U-shaped plaster splint (see fractures of both bones of forearm for details) was applied and left on for from three to five weeks. Massage was begun on the tenth day and passive motion and rotation at the end of the third week.

Pronation was complete in 2 cases and in these 2 supination was also nearly complete. In the other 8 cases pronation was two-thirds normal and supination five-eighths normal.

Fractures of the Shaft of One or Both Bones.—Fracture is usually in the middle or lower third of the forearm, and the radius is usually fractured at a higher level than the ulna. Fracture of a single bone is most frequently due to direct fracture of both bones to indirect violence. Green-stick fractures are more common in the radius than in any other bone. Displacement in any direction may occur, and, if unreduced, is of special importance as affecting the rotation of the forearm. A peculiar displacement is that of supination of the upper fragment of the radius by the biceps when the bone is broken above the insertion of the pronator teres. According to most authors, unless the limb in such case is immobilized in extreme supination a permanent loss of that motion will result. Practically, however, the impairment to supination when the limb is kept in the usual semipronated position is unimportant. Of far greater importance is the total loss of rotation that follows fusion of the two bones even when a lateral enarthrosis appears in the callus, as is rarely the case. The points that favor such a fusion are: (1) persistent displacement of the bones toward each other, (2) excessive callus from insufficient immobilization or imperfect reduction, and (3) the rare occurrence of fracture in both the bones at the same level.

In fractures of a single bone the displacement is usually slight, and the diagnosis may be difficult. A point of local tenderness may be found with either crepitus, false motion, or irregularity of the surface of the bone. In fractures of the ulna alone the head of the radius is often dislocated forward and upward.

Treatment.—Reduction by traction and local pressure, special attention being paid to the correction of any displacement of the bones toward each other, forcing them apart by deep pressure with the finger-tips on the front and back of the forearm. Green-stick fractures must be reduced by forcible bending, even completing the fracture, if necessary. *Circular constriction* of the limb should *never* be applied, for this is a most fruitful source of gangrene. The arm should be placed midway between pronation and supination with the elbow flexed to a right angle.

The best splint is a U-shaped molded plaster splint, which should begin at the base of the fingers on the palmar side, pass up the anterior surface of the arm about the flexed elbow, and down the dorsum to the base of the fingers. This is carefully bound in place, avoiding circular constriction. The patient should be encouraged to move the finger from the start. Firm union occurs in from six to fourteen weeks, but delayed union is quite frequent.

> In fractures of the ulna at its upper **third** with dislocation of upper end of radius the writer urges the abandonment of simple arthrotomy or excision of a portion of the radius in this condition, and advises treatment as follows: In recent cases reduction without operation should first be attempted. The joint should be immobilized in the acutely flexed position and two radiograms from different aspects taken. If the radial head is not in place, or if there is overlapping or angular displacement of the ulna, which would probably later hinder supination and pronation, operation after at least a week has elapsed is indicated. The ulna should first be fixed in proper position, preferably with Lambotte's plate, and the head of the radius then replaced *de visu.* In cases already of long standing, simple **arthrotomy** is useless because the irreducibility is bony in origin, the ulna having become too short for the radius. An **osteotomy** of the ulna should first be done, and this bone fixed in its normal condition, if this is possible; if not, the radius should be reduced primarily, and the ulna then sutured in a corresponding position. **Excision of the radial head** should be done only if reduction has proved impossible. If there has been rectilinear consolidation of the ulna—almost always, however, with some shortening —a choice will have to be made between oblique ulnar osteotomy with open reduction of the radius, and primary excision of the radial head. This point can only be settled by further experience, but, other things being equal, the former procedure seems preferable, since the normal skeletal conditions are preserved. J. Abadie (N. Y. Med. Jour., from Presse méd., Jan. 18, 1913).

Fractures of the Lower End of the Radius (Colles's Fracture).—This is, after fracture of the ribs, the commonest of all fractures. It is generally produced by a fall upon the palm of the hand. The line of fracture runs irregularly across the bone within an inch of its articular edge. In the young it commonly follows the epiphysial line. The lower fragment is tilted back and impacted. It may be comminuted. The upward displacement is not great, but the tilting and crushing carry the styloid process of the radius to a higher level than that of the ulna, which is made prominent by the shifting over of the carpus. The periosteum on the back of the radius remains untorn. The styloid process or shaft of the ulna may be broken. Rarely the internal lateral ligament is torn.

> From 85 to 92 per cent. of Colles's fracture result badly, owing to defective reduction. Elbow-joint fractures that are unsuccessful are those due first to incomplete reduction, those reduced by a bandage, and those having torn-off periosteum. Clinical observation in all cases is the final court of appeals. The writer removed the surgical head of the femur in a boy and interposed soft fascia from within the pelvis. The boy had a perfect joint and perfect control which was an actual demonstration. In a knee-joint the periosteum had no osteogenetic force; hence we must implant bone that had. J. B. Murphy (Trans. Amer. Med. Assoc.; N. Y. Med. Jour., June 15, 1912).

The characteristic symptoms are the so-called "silver-fork" deformity, a backward displacement of the whole hand and the lower end of the radius, producing a swelling over the back of the wrist and a deep crease in the front. The styloid process of the ulna is prominent and lower than that of the radius. Crepitus and mobility are usually absent. There is a line of tenderness along the line of fracture.

> Automobile fractures are cases of fracture of the lower and usually outer end of the radius caused by the sudden and violent reversal of the starting crank of an automobile, the so-called "kick-back." Only those produced indirectly by the force acting through the palm of the hand are meant. The X-ray picture in a typical automobile fracture will show a fracture line in the lower end of the radius below the usual site of a Colles fracture. This line runs either transversely across the bone or, what is more common, obliquely into the joint. There is no impaction, no displacement, and consequently little or no deformity. There is, as a rule, no crepitus, little deformity, swelling, pain, or discoloration. The loss of function also is slight, though rather greater than the other clinical symptoms would call for. Gentle motion can be made; forced ones are painful. There is a distinct point of tenderness on the lower and outer end of the radius, and this clinical sign is always present and shows, in this fracture perhaps more than any other, the value of pressure-point tenderness in the diagnosis of fractures. The diagnosis must often be made from the history and this sign alone. An X-ray is to be taken when possible. In regard to treatment, the less done the better, as a rule. Any attempt to improve the slight deformity is unnecessary. The author's cases proceeded to a speedy and full functional recovery without any manipulations. He recommends immobilizing, and, after, a week, daily massage and motion of the joint. Recovery is usually complete in three weeks. W. H. Winterberg (Calif. Jour. Med., Feb., 1912).

The diagnosis from dislocation is given under that heading.

Treatment.—The simplest way to break up the impaction is for the surgeon to grasp the forearm firmly just above the fracture. With the other hand he then grasps the injured hand, placing his thumb lightly on the back of the lower fragment. Dorsal flexion is made until the patient complains of pain, and then with a sudden movement the dorsal flexion is increased and simultaneously strong pressure is made on the lower fragment. In a moment the fracture begins to give, the dorsal is quickly exchanged for palmar flexion, the wrist being pried backward, and the resultant crepitus announces the dissolution of the impaction. Inspection should then show that the "silver-fork" deformity has disappeared. The impaction once thoroughly broken up, the bones tend to remain reduced, and should be immobilized by anterior and posterior plaster splints, which need not extend so far up the forearm as for fractures of the shaft (*q.v.*). **Massage** is very useful to shorten the convalescence and can best be used if, instead of wooden splints, molded plaster ones are used, extending from the middle of the forearm to the metacarpophalangeal joint both in front and behind. The hand is most comfortable in slight dorsal flexion. Its position bears no particular reference to that of the fragments. A simple band of adhesive plaster around the wrist is said to decrease the prominence of the ulna, and, indeed, seems to be the only splint necessary in some few cases. The fingers must be exercised from the beginning.

> Study of 14 cases in children less than 16 years of age. The signs of the fracture are, perhaps, not quite as typical as in adults, but are sufficiently constant to warrant the paying of special attention to this type of fracture. In but 1 of the author's cases did the plane of separation pass through the epiphysial line. The prognosis is always good in these cases; all the children observed showed complete functional recovery. No plaster cast should be used, splints being uniformly sufficient. Petroff (Revue méd. de la Suisse Romande, Nov., 1912).

Other Fractures Near the Wrist.—Cases have been recorded of reversed Colles's fracture from a fall on the back of the hand. The lower end, or styloid process, of the ulna may be fractured alone. The so-called Barton fracture of the anterior or posterior lip of the articular surface of the radius is merely incident to dislocation of the carpus (*q.v.*).

> An analysis of 214 cases demonstrated that the most common injury at the wrist in cases in which the epiphyses have joined their shafts is a transverse fracture one-half inch above the lower end of the radial bone, the lower fragment being displaced backward, and with or without a fracture of the styloid process of the ulna, while in cases in which the epiphyses are not yet united, the commonest injury is a transverse fracture about one inch above the lower ends of both forearm bones and with both lower fragments displaced backward. Knox (Lancet, Nov. 2, 1912).

FRACTURES OF THE CARPUS.

—Since the advent of the X-ray, fractures of the carpal bones are found to be more common than was formerly supposed. Of these fractures, fracture of the scaphoid and fracture of the scaphoid with dislocation of the semilunar are the most common. Fractures of the os magnum, semilunar, trapezium, cuneiform and pisiform are rare and an X-ray picture is needed for diagnosis.

Fracture of the Carpal Scaphoid.—

Etiology.—A fall or blow upon the ball of the thumb with the wrist in dorsal flexion.

Pathology.—The line of fracture is transverse and usually nearer the proximal portion of the bone. The fragments are more widely separated in ulnar flexion and closer together in radial flexion of the hand. When one fragment is displaced it is usually the proximal fragment and the displacement is anterior.

> Three patients, in each of whom there was a fracture of the carpal scaphoid with secondary injury to the median nerve, as shown by localized anesthesia. In 2 of the patients the history of the accident was clear and indicated that the injury had resulted from a severe bending backward of the hand upon the forearm. This movement, exerted with considerable force, is believed to have caused the damage to the median nerve through stretching. Campbell (Lancet, Nov. 9, 1912).

Symptoms.—Pain in the wrist-joint, limitation of all movements, swelling and tenderness upon digital pressure in the anatomical snuffbox between the thumb extensors, especially in radial flexion of the hand.

Diagnosis.—The X-ray is necessary to confirm the diagnosis.

Prognosis should be guarded. As a rule, there is some limitation of motion and pain on long use.

Treatment.—In cases without displacement, a palmar splint with hand in radial flexion, early **massage,** and **baking.**

Where the proximal fragment is displaced, incision and removal.

Fracture of the Scaphoid with Dislocation of the Semilunar.—The cause is the same as that of scaphoid with some additional force pressing the hyperflexed hand either directly or obliquely toward the radius.

Symptoms.—Pain, disability, tenderness in the snuffbox, and a hard, bony swelling beneath the extensor tendons; shortening of the wrist, and radial deflection of the hand and prominence of the lower end of the ulna.

Treatment.—Excision of the semilunar and displaced proximal fragment of the scaphoid.

The prognosis and after-treatment is the same as in fractures of scaphoid.

Metacarpal Fractures.—The base of the first metacarpal is frequently broken (Bennett's fracture) and is easily recognized.

The other metacarpal fractures usually occur in the third and fourth bone and are caused by direct or indirect violence. The injury is readily recognized. The tendency to displacement is slight.

The X-ray has demonstrated the comparative frequency of fracture of the metacarpal bones. This is especially noteworthy in boys under 18, in whom there is frequently a separation of the epiphysis due to direct violence. Cases of fracture from indirect violence are, however, not unusual. The diagnosis may be difficult without the X-ray, especially when there is much swelling and much tenderness. The points to be observed in diagnosis are crepitus, unnatural mobility, displacement, ecchymosis, and swelling. The prognosis depends very largely upon the intelligence with which the treatment is carried out. Beck's treatment is recommended, which consists in the use of a coaptation splint of short pieces of drainage-tube of suitable size, applied on either side of the fractured bone on the dorsum of the hand, and held in place by a strip of adhesive plaster. Mackenzie (Pract., Oct., 1908).

A favorite splint is made by fastening the hand over a soft ball by means of a strip of adhesive plaster. An anterior splint well padded up in the palm serves equally well.

The best method of treating metacarpal fractures is by a long, palmar splint with adhesive strips at the wrist for counterextension and two strips applied to the finger after the manner of Buck's extension apparatus; pads are placed above and below the line of fracture to prevent displacement.

In fracture of a finger, an important point in the treatment is to maintain the alignment of the phalanx, and especially to guard against rotation of the distal fragment upon its long axis. In a compound fracture, the greatest care must be exercised in procuring absolute surgical cleanliness, since infection spells ruin, necrosis, and suppuration involving functional impairment. Any method of fixation giving complete rest to the part will suffice. A thin, wooden splint, narrower than the finger, is generally recommended, but the author prefers a plaster mold, which can be cut to fit any shape, size, or condition. Jas. Jefferson (Penna. Med. Jour., May, 1912).

Phalangeal fractures are usually compound. The hand may be bound over a roller bandage by means of several strips of adhesive plaster, one for each finger. Straight posterior splints may also be used.

> Case illustrating the necessity of tying a broken finger to its sound neighbor, as otherwise the finger is liable to grow crooked. The displacement from the dressings caused this defect in the author's case, compelling subsequent operative correction. Hohmann (Münch. med. Woch., Aug. 13, 1912).

FRACTURES OF THE PELVIS

may be grouped under seven heads:—

Fractures of the Ring.—Under this title are grouped all fractures that dissolve the continuity of the pelvic ring. Such fractures must, of necessity, be vertical in the main. They are usually caused by a crushing from before backward. The line of fracture usually runs through the upper (just internal to the pectineal eminence) and lower (near its junction to the ischium) rami of the pubic bone. Such a fracture may be bilateral, and associated with a vertical fracture of the sacrum, a separation of the sacroiliac synchondrosis, or a fracture through the ilium behind the acetabulum. These are the double vertical fractures of the pelvis. This double fracture may also occur from a fall on the foot, or the same cause may dislocate the os innominatum at both symphyses. Or it may cause a radiating fracture of the acetabulum with or without penetration of the femoral head through the bone. Fractures of the ring are usually comminuted. Displacement of small fragments or a general mobility, with crepitus, of the whole pelvis may often be recognized. In double vertical fracture the fractured bone is often tilted; so that the superior strait is widened, the inferior strait narrowed, and the limb apparently shortened. Complications are usual and severe. Rupture of the membranous or prostatic urethra is almost inevitable, and the other common injuries are rupture of the pelvic vessels, the rectum, the bladder, and the ureters.

Treatment.—The associated injuries demand immediate attention. For the fracture itself rest in bed with even compression all around the pelvis is all that can be done, except in cases of tilting of the os innominatum, in which traction should be made as after fracture of the thigh.

> There is a wide divergence of the outcome in cases of fracture of the pelvis, some patients dying of shock from the serious injury, others surviving with severe complications, while in others the fracture behaves and heals like the fracture of any bone without further trouble. In 4 cases reported the fracture healed in a plaster cast without complications in 2 cases, but complications and injury of viscera soon proved fatal in the others. Bard (Lemana Medica, May 2, 1912).

Transverse fracture of the sacrum results from direct violence. The angular displacement forward may be corrected by pressure from within the bowel. A tendency to recurrence has been prevented by the adaptation of the urethral striated cannula to the rectum.

Coccygeal fracture resembles dislocation. It is rarely observed.

Fractures of the ilium are comparatively frequent and the result of direct violence. The crest of the various spinous processes may be broken. The treatment is rest in bed.

Fracture of the ischium in any of its parts is rare.

> Case of fracture of the tuberosity of the ischium due to muscular action. This variety of fracture is comparatively uncommon. The only mention made of it by Scudder in the latest edition of his work is the statement that it is extremely rare. Stimpson mentions 6 cases collected by Malgaigne. Cotton in his recent book states he has no doubt that it may occur, and he has seen a number of cases in which that diagnosis had been made, but none in which it was justified.
>
> The patient while racing felt something crack and fell to the ground. He was able to get up and walk, but there was extreme soreness and pain in the left buttock, which persisted, though to a less degree, after the subsidence of the acute symptoms. He was unable to sit on a hard seat, and there was pain on bending forward and on standing in certain positions, and movements of the left leg caused pain and audible grating. On palpation a hard, movable body apparently 4 or 5 cm. in length, could be felt deep in the tissues. The X-ray showed that this was a detached fragment of the tuberosity of the ischium displaced by the pull of the hamstring muscles attached to it, and the strong action of these muscles had evidently caused the fracture three years before. The fragment was removed under a general anesthetic. The recovery was uneventful, and except for a slight soreness in the left buttock, the patient's condition was satisfactory. J. M. Berry (Jour. Amer. Med. Assoc., Oct. 19, 1912).

Fracture of the pubes not extending across both rami is also infrequently met with.

Fracture of the Acetabulum.—Fracture of the rim may complicate dislocation of the hip and may be so extensive as to favor recurrence. Stellate fracture may be indicated by pain on pressure through the thigh. If the head of the femur has perforated the acetabulum it should be replaced by traction.

FRACTURES OF THE FEMUR.

Fracture of the Neck of the Femur.—The division of these fractures into intracapsular and extracapsular has no clinical value and is not borne out by post-mortem findings. The more accurate classification is: (1) fractures through the narrow part of the neck, and (2) fractures at the base of the neck. Clinically, it is often impossible and never necessary to distinguish between the two.

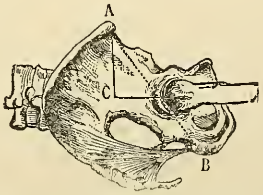


Fig. 7.—*A-C-D*, Bryant's iliofemoral triangle. *A-B*, Nelaton's line. (*Owen*, "*American Textbook of Surgery*.)

Symptoms.—The chief deformity is shortening of the limb with eversion. The eversion is usually slight, often absent, and rarely exchanged for inversion. The shortening may appear at once or may only come on gradually. In the latter case, under appropriate treatment the shortening may never appear at all. In measuring for shortening the greatest care must be taken to compare the limbs when placed in exactly similar positions. There is also a fullness in the outer part of Scarpa's triangle, and the fascia lata above the great trochanter is relaxed, as compared with the other side, on account of the elevation of the trochanter. Normally the upper border of the great trochanter just touches Nélaton's line drawn from the anterior superior spine of the ilium to the tuberosity of the ischium (*A-B,* Fig. 7). In fracture of the neck, with shortening, the trochanter rises above this line, and the amount of displacement may be measured by means of Bryant's iliofemoral triangle, variations in the length of the line *C-D* (which is at right angles to *A-C,* a perpendicular dropped from the anterior superior spine of the ilium) indicating the displacement of the trochanter. If the trochanter is split, it is broadened in comparison with its fellow.

Crepitus can rarely be obtained. Pain may be diffuse, but pressure over the neck of the femur is likely to be painful, as is upward pressure of the femur. A few cases are reported in which the patient has walked on the limb, but usually loss of function is complete and all the movements of the joint restricted.

The history of a typical case is as follows: An elderly person, preferably a woman, while walking about, stumbles and falls to the floor, with perhaps little violence. She cannot rise, and complains that every movement of the hip is painful. Examination will reveal symptoms as indicated above.

Diagnosis.—The diagnosis between the fractures through the neck and those at the base is often impossible. Splitting of the trochanter is a sure sign of the latter, while after the former it is believed that shortening is more likely to be secondary.

> The X-ray has demonstrated the incorrectness of the old idea that fracture of the neck of the femur is very rare in the young. The writers have encountered 9 typical cases of fracture of this kind and review the literature on the subject. The symptoms in the young are generally the same as in adults, but sometimes there may be no pain, deformity or disturbance in walking. This is liable to be the case with an incomplete fracture, and the patients may have forgotten their traumatism when coxa vara develops later. The insignificance of the trauma causing the fracture is frequently mentioned in the cases on record: this seems to be peculiar to fracture of the neck of the femur in the young and in the aged. Worms and Hamant (Revue de Chir., Oct., 1912).

In dislocation the motions of the limb are restricted in certain definite directions and the head can be felt while in the usual dorsal dislocation; the emptiness of the acetabulum may be determined by pressure on Scarpa's triangle.

In subtrochanteric fractures the trochanter does not share in gentle rotation imparted to the shaft.

In old persons it is not rarely an absolute impossibility to differentiate contusion of the hip from fracture of the neck of the femur. In such a case, when the sole symptoms are pain and disability, treatment for fracture should be instituted without the slightest hesitation, the patient being bedridden in any event, and this treatment should be continued for at least three weeks and until all pain and soreness have disappeared. Thus, if it turns out to be a contused hip, the patient has not been unduly inconvenienced, while if it be a fracture he has been given the best chances of recovery and the surgeon has, perhaps, avoided a suit for malpractice.

> Four cases of fracture of the floor of the acetabulum. This injury is usually due to a fall from a height, the patient landing on the side and the greater trochanter receiving the bulk of the impact. The trochanter, unless the patient is old, is stronger than the

acetabular floor, which is more apt to give way. The diagnosis is made by careful comparison of the two sides, measurements, rectal examination, which may show some bulging over the site of the acetabulum, and the X-ray. The catheter will disclose injury of the bladder, if present, and injury of the bowel should be sought for and treated if found, and hemorrhage controlled. The fracture is then reduced and extension applied in the axis of the limb in conjunction with lateral traction upon the femoral neck. A cast is applied after a few days from the toes to the costal margin. After union is obtained **massage** and **passive movements** are employed. Skillern and Pancoast (Annals of Surg., Jan., 1912).

Etiology.—As has already been indicated, fractures of the neck of the femur is usually caused by a comparatively slight injury to an old person, usually a woman. In the young a much greater amount of violence is required to break the bone.

Pathology.—In fractures through the neck the cancellous tissue is crushed, but impaction is rare. The head of the bone may be splintered. As a portion of the periosteum habitually remains untorn, the vitality of the head is insured thereby, and union, fibrous at least, may be expected. Fractures at the base are likely to be impacted and the line of fracture may split the great trochanter. The greatest impaction is usually behind; hence the thigh tends to rotate outward. The callus is often excessive.

Prognosis.—The prognosis, even as regards life, is far from cheering. The aged and feeble patient is liable to pass into a cachectic or demented state and thus to fade away, often hypostatic pneumonia.

Or he may die in a few days by the shock. After he has passed the third week, however, the prognosis is good. As to union, it may be fibrous or fail entirely, such a result entailing in some cases no disability to speak of beyond the inconvenience of a shortened limb, while in others locomotion may be entirely lost.

Treatment.—The first indication is to save the patient's life, and to this all else must be subordinate. Such splints should be applied as will most promote the patient's comfort, and the disturbance of repeated measurement and redressing avoided. Careful nursing, feeding, and stimulating are of capital importance. Premonitory signs of dementia must be watched for, and if the patient seems to be failing he must be gotten out of bed, whether his thigh has united or not. In this event the hip should be disturbed as little as possible and the patient allowed to recline in a wheel-chair. Pressure over the trochanter will encourage union, the pressure to be made by a pad under a pelvic band worn as tight as is compatible with the patient's comfort.

Energetic manipulations either for the purpose of eliciting crepitus or correcting deformity have a tendency to tear the periosteum still farther and to separate impacted fragments. Such shortening or eversion as cannot be overcome by the traction splint is best left uncorrected, lest non-union be courted. Traction should be continued for at least five weeks and the patient kept in bed a week longer. The best traction splints are Buck's and Hodgen's. Buck's is the more convenient for the surgeon, permitting accurate examination and measurement without disturbing the dressing; but Hodgen's is much more convenient for the patient, and should be preferred for the aged.

In **Buck's extension** the traction is made by weight and pulley over the foot of the bed, which may be raised for counter-extension. It is applied as follows: A strip of stout adhesive plaster (the so-called "moleskin-diachylon" plaster, although it is rather difficult to apply, requiring to be heated before it will adhere,—and if overheated it will blister the skin,—is least irritating), four inches wide and long enough to reach from well above the knee loosely around the sole of the foot and back above the knee again, is cut as shown in Fig. 8, and a small perforated block of wood placed at its center. Through the hole in the wood and a corresponding one in the plaster a cord is passed, so knotted at the end that it cannot slip through. The edges of the plaster are now turned down over the block and each other (Fig. 9). A roller bandage (preferably of flannel) is applied to the foot and lower third of the leg, the adhesive plaster applied to the sides of the leg and thigh above it, and the bandage continued up over the plaster (Fig. 10). The cord is then carried over the pulley at the foot of the bed and attached to a weight of from 5 to 20 pounds, the heavier weights only being applied to robust and young patients whose shortening is not done away with by the lighter ones. Outward rotation is prevented by employing Volkmann's sliding rest (Fig. 11), and sand-bags along the outer side of the thigh.

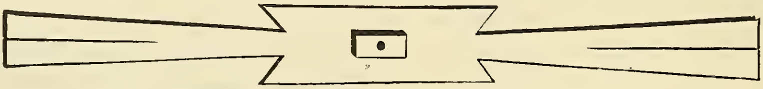


Fig. 8.—Adhesive plaster cut for Buck's extension. (*Stimson.*)

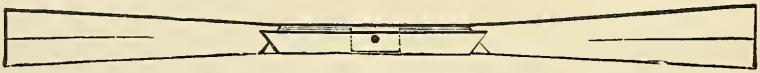


Fig. 9.—Adhesive plaster folded for Buck's extension. (*Stimson.*)

Hodgen's splint (Fig. 12) consists of two iron rods slightly bent at the connection of their upper and middle thirds and attached together by a straight bar at the lower ends and a curved one at the upper. The limb being attired as for Buck's extension (Fig. 10) the cord is attached to the straight cross-bar and a number of narrow compresses or pieces of bandage are pinned to one rod, passed under the limb, and pinned to the other in such a way as to give uniform support to the limb when it is raised from the bed. The apparatus is sup-

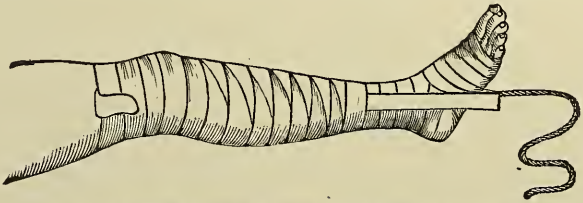


Fig. 10.—Adhesive plaster applied for extension (*Stimson.*)

ported by two loops tied to a cord which is attached to a crane at a point at least four feet above the bed and at an angle of about ten degrees from the vertical.

Traction hip-splints, such as are used in hip-joint disease, have also been applied here. Their use is certainly a great convenience and will doubtless be more frequent in future. Unfortunately, however, they cannot be used by the very ones who need them most—the aged and infirm.

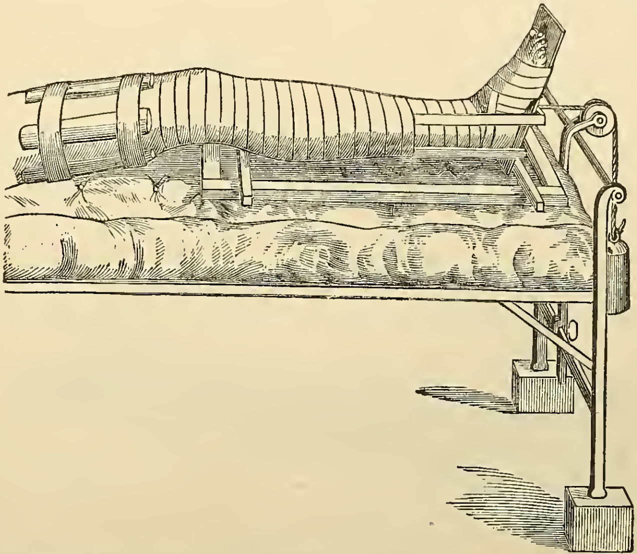


Fig. 11.—Volkmann's sliding rest for fracture of the thigh. (*American Textbook of Surgery.*)

When the shortening has once been reduced some surgeons prefer to apply a plaster splint from waist to ankle at once. With such a splint pressure may be made over the trochanter through a fenestra to encourage union.

For the treatment of recent fractures of the hip, the writer greatly prefers that originally suggested by Phillips, which consists of the usual longitudinal traction with weights and sand-bags or other device to hold the foot vertical, supplemented by lateral traction by a weight over the side of the bed, drawing the upper portion of the thigh out. He has also obtained good results by the use of plaster of Paris, putting the limb up in extreme abduction as advised by Whitman in cases of children. Of these two methods the lateral traction is the one usually easier to apply and carry out. G. G. Davis (Annals of Surg., Oct., 1912).

Excision of the head for non-union has been done with varying success, but should not be attempted until the failure of a prolonged course of treatment by ambulatory traction, combined with firm pressure over the trochanter (Schaefer), has shown that union is impossible.

Fractures of the Great Trochanter.—The trochanter alone may be separated by direct violence, or the line of fracture may pass through the neck above the lesser trochanter and thence through the lower part of the great trochanter. In such cases there are the usual signs of fracture of the neck, to which are added independent mobility of the trochanter and a prominent tender spot in front of it.

Treatment.—**Hodgen's splint.**

Fracture of the Shaft.—Under this head may be included both "subtrochanteric" and "supracondylar" fractures. The line of fracture is usually oblique and there is both overriding and angular deformity. As the line of fracture usually runs downward and forward the angle is made by the posterior fragments being drawn up behind it. The upper fragment is often rotated outward. In fractures of the upper third the upper fragment is usually abducted. In those of the lower third its sharp point is liable to pierce the quadriceps and even the skin. The shortening may be determined by measurement, the abnormal mobility by gently elevating the limb beneath the point of fracture. The trochanter is not displaced upward. A complicating synovitis of the knee is common, laceration of the great vessels rare.

Prognosis.—Shortening of about an inch should be expected.

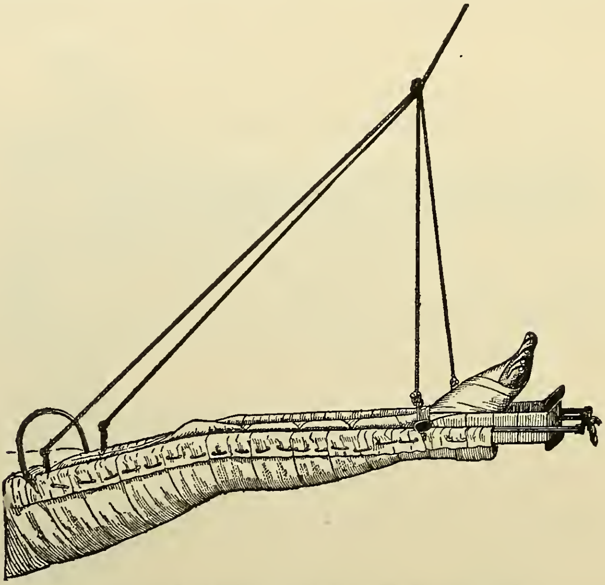


Fig. 12.—Hodgen's splint. (*American Textbook of Surgery.*)

Treatment.—Reduction is to be made gently. In fractures of the lower third, if the upper fragment has pierced the quadriceps and cannot be disengaged by traction with the knee and hip strongly flexed, reduction must be made through a free incision.

Immobilization is best made by Hodgen's splint, which, while it does not immobilize quite as fully as Buck's, permits much more liberty to the patient, and can be adjusted in such a position as to avoid deformity more surely, namely: flexion and abduction of the hip for high fractures and flexion of the knee for low ones. With Buck's extension it is particularly essential that the bed should be made flat by a "fracture-board" placed under the mattress. If the fracture is near the center of the shaft coaptation splints may be used with advantage. In England a long side-splint with traction is a favorite dressing. It is very inconvenient. The tendency to outward rotation in the upper fragment is best opposed by a hard cushion under the great trochanter. Traction should be maintained for six weeks, the patient being kept under constant observation. Then he should be kept on crutches with a plaster-of-Paris splint from waist to ankle for about three weeks longer. If union is fibrous the irritation of walking in a plaster splint should be beneficial, but great care must be taken to avoid angular deformity.

> A study of 760 tabulated cases of fracture of the shaft of the femur showed that in most cases treatment by some form of traction enables the patient to resume his occupation and function without serious detriment. In selected cases, where it is impracticable to restore the fragments to their proper position, and where mechanical means have failed within a reasonable time to produce proper restitution of the fragments, the open method may be employed, but then only by an experienced surgeon, one who habitually employs most thorough aseptic methods. The results may be considered good if the measurements show no more than an inch of shortening, provided there is no inversion or eversion of the foot from angulation of the fragments. Estes (Annals of Surg., July, 1912).

When the traction does not correct the deformity in ten days, open operation with reduction should be done (see general treatment of fractures for detail, etc.).

Ambulatory treatment as for fractures of the neck of the femur has proved satisfactory. Children under 10 are best treated by vertical suspension of both legs. The pelvis should be elevated about two fingerbreadths above the bed, thus making counterextension.

For compound fractures the double-inclined plane (Fig. 13) is often most convenient. It affords no traction, but the loss of bone substance by comminution usually renders traction unnecessary. In other cases Smith's anterior splint, which acts like a suspended double-inclined plane, is more appropriate.

Fractures of the Lower End of the Femur.—Epiphysiolysis is more frequent here than at any other point. It occurs as late as the twentieth year, usually from torsion or hyperextension of the leg. Associated injury to the vessels is common. The treatment is the same as for fractures of the shaft.

Fracture of one condyle is usually due to direct violence. Immobilization should be made with the knee extended.

Intercondyloid fracture presents the same features as intercondyloid fracture of the humerus.

TREATMENT.—Any fracture of the femur involving the knee-joint should be immobilized in extension. A molded posterior splint and slight traction will usually prove satisfactory as far as the fracture is concerned; but the chief dangers are gangrene from injury to the popliteal vessels, and ankylosis or suppuration in the knee-joint. Some subsequent stiffness in the knee is always to be anticipated.

Fracture of the Patella.—This is common between the ages of 20 and 50. It may be comminuted when due to direct violence. Rarely it is vertical. Ordinarily it is transverse and due to muscular action, as in jumping or avoiding a fall. The sudden pull of the quadriceps snaps the bone. The snap and a sharp pain are felt by the patient, and extension of the leg is almost completely lost. The gap between the fragments is readily palpable, but is usually small at first, for the lateral ligamentous attachments of the upper fragment prevent the quadriceps from drawing it up the thigh. The joint becomes distended with effused blood. The periosteum over the patella is torn irregularly and a fringe of it drops between the fragments.

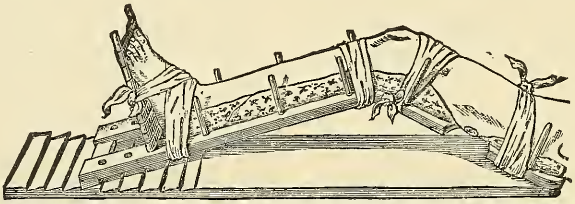


Fig. 13.—Esmarch's double-inclined plane. (*Esmarch and Kawalzig.*)

> Fracture of the sesamoid bones, outside of the patella, is rare, only 16 cases having been reported; 14 of these were in males. In the writer's case the mishap was caused by having the foot trampled on while dancing, the acute symptoms being succeeded by residual soreness and tenderness and pain on walking. The X-ray showed fracture of the tibial sesamoid bone with separation of the fragments, but no displacement. Excision of the fragments and suture of the tendon to the capsule entirely removed all pain and disability. Muller (Annals of Surg., Jan., 1912).

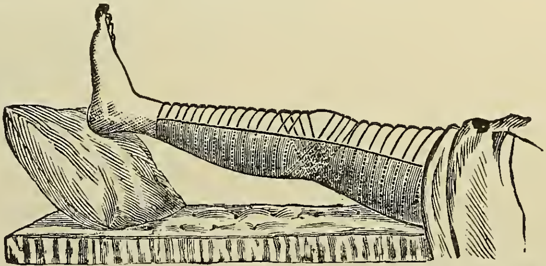


Fig. 14.—Hamilton's dressing for fracture of the patella. The final turns of the roller in front of the knee are not shown in cut. (*American Textbook of Surgery.*)

Prognosis.—In the absence of treatment or from its inefficient application the two fragments will be drawn farther apart by the retraction of both the ligamentum patellæ and the quadriceps. Adhesions from organized blood-clot and lacerated ligaments immobilize the joint more or less completely, and extension is still farther impaired by adhesions between the upper fragment and the femur and by the loss of coaptation between the patella and the condyles.

Treatment.—Non-operative treatment consists in causing the absorption of the fluid in the joint by pressure (massage is of little service) and then immobilizing the fragments until union has taken place. A Martin bandage should be applied with as much pressure as the patient can bear for four to six days, and may be continued for a fortnight if it holds the fragments in good position. During this time the patient is kept in bed with the knee extended. A posterior molded splint is then applied from the ankle to near the hip and is bandaged in place as shown in Fig. 14, the turns of the bandage about the knee pressing the tissues above and below the fragments toward each other,—these may be reinforced by strips of adhesive plaster,—and finally a few turns are taken over the fracture to prevent tilting forward of the fragments. The dressing must be worn for a month and frequently inspected and altered if necessary. At the end of this time an immobilizing plaster bandage is applied, and the patient allowed to go about on crutches. This splint must be worn for a month, not that union will become much firmer, but so as to accustom the patient to walking about, and to loosen the adhesions a little, that the bone may not be refractured by another fall or slip. During this time **massage** may prove useful, and to that end the splint may be split anteriorly, removed daily, the limb massaged, and the splint replaced and held firmly by a roller bandage. At the end of the second month the patient is discharged, but advised to walk with care. Various splints have been devised to secure immobilization of the knee and coaptation of the fragments, but they present no advantages over the above method. A plaster bandage should never be applied until union has taken place. Malgaigne's hooks and their various modifications have had great vogue. The principle involved is the holding of the fragments in apposition by means of sharp hooks, which may be inserted into the upper and lower edges of the bone and drawn together by a screw. The danger in their use is that suppuration provoked at the points of puncture may travel into the joint either through the lymphatics or the cellular planes, especially if there is much effusion of blood. Finally, aspiration has been used—with strictest asepsis—to empty the joint more rapidly than is possible by pressure.

Operative measures include various sutures,—mediate, immediate, subcutaneous,—the trimming off of the fringe interposed between the fragments, and washing out the joint. The following operation is preferred,—if operative treatment is elected: Through a median incision extending a little above and below the fragments, sharp hooks are inserted into each fragment, drawing them apart, and the joint is flushed with sterile "normal" salt. The whole line of fracture is now exposed by lateral retraction of the flaps, and, *without touching the tissues with his fingers,* the surgeon elevates any interposed fascia and periosteum and holds them and the fragments in place with a few fine catgut sutures. A suture or two may also be taken in the capsule of the joint, if it is widely torn. These sutures may be reinforced by a single silk or stout catgut suture passed through the quadriceps tendon and the ligamentum patellæ and crossing the front of the bone. The skin is then sutured with silk. No drainage. A plaster bandage is applied and the patient sent to bed, where he remains with his foot elevated for a week. The splint is then removed, the skin sutures taken out, and the splint reapplied. A few days later the patient gets up on crutches. These and the splints he wears for a month. The splint is then cut down again, and he wears it in the daytime alone for another month. No further treatment is required. The operation may be done under **cocaine.** The reasons for preferring this operation to any other is that it fulfills the indications of washing out the joint, complete reduction, and firm immobilization in a thoroughly aseptic manner, and leaves behind no foreign body in the joint to set up suppuration or irritation. By keeping his hands from contact with the tissues the surgeon makes the operation as safe as, and safer than, any subcutaneous one, as has been borne out by the experience of 90 consecutive cases without suppuration (Stimson).

The Choice of Treatment.—The results of immobilization vary from a perfect functional result with about one-fourth inch separation to absolute loss of function with wide separation or stiffness in the joint. Such results are attained within about six months. Operation may give a perfect result with linear union, but, on the other hand, postoperative suppuration in the knee-joint may prove fatal. If the operation is successful the patient saves about two months of convalescence and a great many of the doubts and annoyances incident to mechanical treatment. Therefore the operation is to be preferred, if the risks of suppuration can be absolutely eliminated. Such is the case only when the surgeon is sure of his own cleanliness, as well as that of his assistants and instruments, is conversant with operative and aseptic technique, and is sure to keep his hands out of the wound. Under such conditions operation is to be elected, with the patient's concurrence.

If function is impaired by failure of union, operation is the only resource. For lengthening the contracted quadriceps its tendon may be nicked at the more tense places, and its lower fibers may be elevated from the femur. Care must be taken, however, not to impair the vitality of the tendon and the fragment of the patella attached to it.

FRACTURES OF THE LEG.—Upper End.—Both bones may be fractured, or else the tibia alone. The avulsion of the spine of the tibia by the crucial ligaments is merely a complication of dislocation. A few cases of epiphysiolysis and longitudinal fracture of the tibia have been noted. If the line of fracture runs into the joint its functions may be impaired, and a tendency to displacement with a resultant genu varum or valgum must be foreseen and prevented by immobilization. Permanent traction may be necessary when there is much comminution.

> The writer found only 2 cases of uncomplicated fracture of the posterior tibial margin on record, and reports a third. While X-ray examination is the final and decisive step in the diagnosis, the presence of this lesion may be suspected where the following three signs are combined: Swelling and ecchymosis on the outer aspect of the lower portion of the leg; sharp pain upon pressure on the posterior tibial surface in the depression between the outer malleolus and tendo Achillis; hyperextension of the foot, with inability to return the foot to a right angle. The prognosis is good with massage, rest in bed, and elevation. Quénu (Revue de chir., Sept., 1912).

Avulsion of the tubercle of the tibia is caused by muscular action quite as is fracture of the patella. Recovery of function may be expected if the leg is immobilized in extension on the posterior molded splint and the fragment retained in place by adhesive plaster.

Shaft.—The usual seat of fracture is at the junction of the middle and lower thirds, the fibula being fractured higher than the tibia. The tibia lies so near the surface of the limb that a diagnosis of its fractures is usually to be made by palpation. This subcutaneous situation also serves to make compound fractures frequent. If the tibia is fractured an accurate diagnosis of fracture of the fibula, often very difficult without the aid of the fluoroscope, need not be made. Fracture of the fibula alone may be made out by a localized point of tenderness elicited by direct pressure or pressure elsewhere along the shaft of the bone.

Edema and neuralgia are exceptionally likely to complicate convalescence from fractures of this region.

Treatment.—Reduction is accomplished by traction with the knee flexed to relax the gastrocnemius. A simple method of treatment is to keep the limb in a Volkmann splint for a few days until the primary swelling has disappeared, when a plaster bandage is applied from the toes to the knee, and changed every ten days until union takes place,—the sixth week.

Should bony union be delayed, the irritation of bearing some weight on the limb in its plaster incasement may prove beneficial. From the time of the application of the plaster splint the patient gets about on crutches. If it is wished to have him about from the first the Volkmann splint may be replaced by a twin posterior molded splint, the two halves of which, when they reach the ankle, diverge to cross each other on the dorsum of the foot.

The subject of ambulatory treatment has already been dealt with in the chapter on general treatment.

Compound fractures are best dressed through a Volkmann or fenestrated plaster splint.

Lower End.—Fracture of the shafts of both bones low down and irregular comminuted fractures require immobilization with the foot at right angle to the leg. Primary amputation is indicated for badly comminuted compound fractures. The common fractures here are fractures by eversion and abduction (Pott's) and fractures by inversion (external malleolus and rarely the internal one).

Study of fractures of the lower extremities of the tibia and fibula, based on radiographs in 146 cases. Displacement of the foot results from lesions involving the projecting lateral margins of the mortise, *i.e.*, the malleoli; if, in addition, the bony edges of the vault of the mortise (formed by the lower end of the tibia) are torn asunder, displacement is further accentuated, while if diastasis of the tibia and fibula occurs, owing to rupture of the intervening ligament, displacement is extreme. Separation of the bones, however, is not characteristic of any specific kind of fracture, but may occur as a complication in every variety. It merely serves as an indication of an injury to the soft tissues which the X-rays cannot render discernible. E. Quénu (Revue de chir.. Jan., 1912).

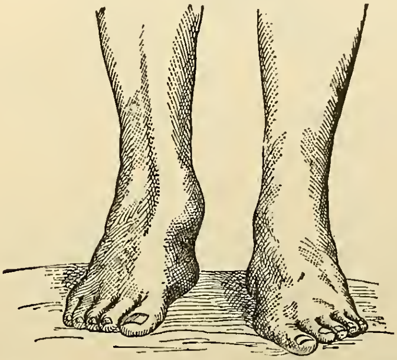


Fig. 15.—Pott's fracture, showing outward displacement. (*American Textbook of Surgery.*)

Pott's Fracture.—This is the commonest fracture of this region. It is caused by eversion and abduction of the foot. The outward and backward displacement of the foot is typical (Figs. 15 and 16). Lateral mobility in the ankle-joint, combined with points of tenderness over the internal malleolus, over the lumen, tibiofibular articulation in front and over the fibula above the malleolus are pathognomonic signs of this fracture. These tender points lie over the then typical lines of fracture, as shown diagrammatically in Fig. 17. The posterior portion of the articular surface of the tibia may also be crushed. Rupture of the deltoid and tibiofibular ligaments may replace the tibial fractures. The typical deformity is caused by the loss of the normal support to the inner side of the foot, and tibiofibular diastasis, which allows the astragalus to slip backward, sometimes so far that it may be quite behind the tibia. If the displacement is not great the patient can walk, though painfully. The fracture of the internal malleolus may be compound.

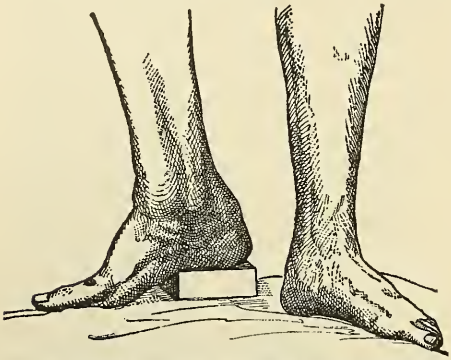


Fig. 16.—Pott's fracture, showing also backward displacement. (*American Textbook of Surgery.*)

Treatment.—To effect reduction the foot must be forced forward and inward, and immobilized in inversion. To maintain reduction posterior and internal plaster-of-Paris splints are very serviceable, the former to extend from the upper third of the leg to the toes, the latter from the same level down to and around the foot, ending at the outer side of the dorsum, the so-called "stirrup-splint." In uncomplicated cases the patient may be allowed to get about on crutches as soon as the primary swelling has abated—a new splint being then necessary—and after that need only be seen often enough to forestall any recurrence of the deformity. It is in Pott's fracture that ambulatory splints are most likely to be of practical use. Some patients can walk with only the support of a shoe, for, as we have seen, the deformity is angular, outward, and backward, and as long as this angular deformity is prevented the functions of the limb are but little impaired. A plaster incasement fortified on the outer side and behind may meet the indications very satisfactorily. It should extend from the toes almost to the knee and be firm and heavy.

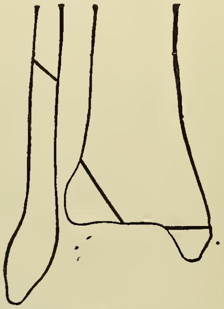


Fig. 17.—Usual three lines of fracture in Pott's fracture at ankle. (*Stimson.*)

If the fragment of the internal malleolus cannot be reduced the knife must be resorted to.

While the results that follow careful treatment are perfectly satisfactory, old unreduced fractures are very troublesome. They may be improved and sometimes cured by supramalleolar osteotomy, or, better, by opening both sides of the joint, chiseling through the old lines of fracture, removing obstructing callus, and reducing the fracture as though it were a recent one.

Fracture of the External Malleolus.—This occurs by the opposite force from that which produces Pott's fracture, namely: inversion of the foot. If, as is usually the case, the fibula alone is broken, or the fibula and the tip of the internal malleolus are broken, it is sufficient to immobilize the foot while it is pressed well inward to prevent widening of the mortise. But if the lower end of the tibia is broken obliquely across, as sometimes occurs, special attention should be paid to the backward displacement.

FRACTURES OF THE FOOT.—**Fractures of the Astragalus.**—This is usually associated with fracture of the os calcis, being caused by a fall on the foot. If there is no displacement the skiagraph is required for diagnosis, and the only treatment is immobilization of the foot. If, however, a fragment is displaced and cannot be reduced, or if the bone is crushed, the fragments had best all be removed, a complete excision of the bone giving a very satisfactory result.

Fractures of the Calcaneum.—This may occur from direct violence, from strain on the plantar ligaments, and from forcible action of the muscles of the calf, putting the tendo Achillis on the stretch. Three weeks are required for solid union. If the fracture separates the sustentaculum tali, the limb must be immobilized with both knee and ankle flexed.

Four consecutive cases of fracture of the calcaneum, in which ecchymosis appeared beneath the plantar arch. It was observed soon after the injury, and always remained distinct from other ecchymotic areas, the marginal portions of the foot never being similarly involved. Heretofore, late appearance and perimalleolar situation have been considered the chief characteristics of the ecchymosis in this form of injury. The writer's observations show that this view is not wholly correct. In 2 cases, in which there was no appreciable bony deformity, crepitus, or localized pain, the plantar ecchymosis proved of great diagnostic value. One of the cases showed also that digitoplantar ecchymosis, *i.e.*, ecchymosis at the bases of the metatarsals and along the lateral surfaces of the toes, hitherto considered pathognomonic of metatarsal fracture, may occur in fracture of the os calcis without involvement of the metatarsals. H. Mondor (N. Y. Med. Jour., from Presse méd., Dec. 28, 1912).

Metatarsal Fractures.—Rest, elevation, and massage will suffice for the cure of single fractures. Multiple fractures require a splint.

Lewis A. Stimson,
and
J. M. Hitzrot,
New York.

FRAMBESIA. See Yaws.

FREEZING.—Freezing may affect the entire body; or, only a part of the body may be involved, as instanced by *frost-bite.* There are three degrees of frost-bite: (1) erythema, or redness; (2) blistering; (3) gangrene. A chilblain is a frost-bite of the first degree where the redness clears up in a few days, but reappears again upon exposure. Chilblain is treated under Pernio.

SYMPTOMS OF FREEZING OF BODY.—Cold is primarily a stimulant, secondarily a depressant to the body cells. After prolonged exposure, drowsiness and numbness are experienced. The body is pale, the blood being driven to the internal organs, which become markedly congested. Finally, the individual falls into a deep sleep, the pupils become dilated, the pulse slow, the respirations slow and stertorous. The body is cold and finally death occurs.

SYMPTOMS OF FROST-BITES.—Freezing first causes a numbness of the parts, followed later by an anesthesia. There is a feeling of weight, coldness, extreme pallor, and, early, a sense of prickling or tingling. If the cold is very intense and applied suddenly the parts may have a mottled appearance. When the parts are warmed, there is extreme itching and burning of the parts, together with redness and swelling.

There is great swelling and lividity of the parts in frost-bites of the second degree, followed later by the formation of blisters. Often ulceration or gangrene follows. An ulcer due to this cause is usually superficial and is difficult to heal. The necrotic tissues are moist and the seat of a thin, ichorous discharge. The surrounding tissues are usually quite inflamed. In frost-bites of the third degree the part is pale and insensitive. There is sometimes excruciating pain in the parts above. The part is cold, edematous, and swollen, but later becomes discolored and shrivelled and a line of demarcation forms. (See GANGRENE, next page.)

TREATMENT OF FREEZING OF ENTIRE BODY.—The patient should first be taken into a cold room and **gentle friction with cold cloths** used. The temperature of the room should be gradually raised as the circulation and respiration return to normal. The friction should be gradually increased and **brandy** or **spirit of camphor** may be used. Later brandy may be given by mouth or by rectum, the patient covered lightly and the extremities elevated. **Artificial respiration** should be used if needed. Warm broths and **warm drinks** should be given as the patient recovers.

TREATMENT OF FROST-BITES.—In frost-bites of the first degree the parts should be **rubbed with ice-water** or **snow.** Recent observations have suggested, however, that **warmth to the parts** is more efficient. As the circulation returns to normal the temperature of the room should gradually be raised, and the parts rubbed either with the hand or with a warm solution. In frost-bites of the second degree, especially with marked inflammatory reaction, **free incisions** should be made. **Silver nitrate** or **tincture of iodine** may be painted on the part. Ulcers should be treated antiseptically, the same measures being used as in ulcers due to any other cause. When gangrene occurs the indications given in the article on GANGRENE should be followed.

In all cases the bowels should be properly regulated and all secretions of the body improved. A light, nutritious **diet** and easily digested food should be given and the general health improved by the use of **tonics.** H.

FREEZING, Local Treatment by, or CRYOTHERAPY. See ETHER, ETHYL CHLORIDE, LIQUID AIR, and, for Carbonic Acid Snow, REFRIGERATION.

FROST-BITE. See FREEZING, EFFECTS OF; and PERNIO.

FURUNCLE. See SKIN, SURGICAL DISEASES OF.

G

GALLIC ACID.—Gallic acid occurs as fine, needle-like crystals, whitish in color, odorless, and having an astringent, slightly acid taste. It is soluble in about 100 parts of water, 5 parts of alcohol and 40 parts of ether. It is incompatible with all the ferric salts, ammonia, silver salts, lead acetate, and potassium chlorate or permanganate.

PREPARATIONS AND DOSES.—*Acididum gallicum* (gallic acid) is given in the dose of from 5 to 20 grains (0.3 to 1.3 Gm.).

The ointment of gallic acid (*unguentum acidi gallici*) is employed for local applications.

PHYSIOLOGICAL ACTION.—Gallic acid acts as an antiseptic, astringent and hemostatic, and is eliminated by the kidneys. It is also mildly antiseptic.

THERAPEUTICS.—Gallic acid may be used externally in **epistaxis; hemorrhoids;** certain skin diseases, especially **psoriasis** and **alopecia,** and may be applied locally to **ulcers** which are actively discharging.

Internally, gallic acid is said to be of value in **diabetes insipidus** and may be given in combination with opium. It may also be used in **night-sweats,** in **intestinal hemorrhage,** and in **diarrhea,** due to atony of the intestinal glands. H.

GAMBIR.

GAMBIR.—Gambir (or *catechu*) is an extract from the leaves of the *Ourouparia gambir.* It has a dark reddish-brown color, an astringent taste leaving a sensation of sweetness, and is insoluble in water. It is incompatible with the iron compounds, bichloride of mercury, sulphate of zinc and lime water.

PREPARATIONS AND DOSES.—The *Tinctura gambir composita* (compound tincture of gambir) is given in doses of from 1 to 2 fluidrams (4 to 8 c.c.). *Powdered gambir* (not official) may be given in the dose of from 20 to 30 grains (1.3 to 2 Gm.).

Trochisci gambir (gambir troches) are also official.

PHYSIOLOGICAL ACTION AND THERAPEUTICS.—Gambir is an astringent and a hemostatic, considerably used as a component of mouth-washes, in conditions in which **spongy gums** are present. The troches are also of value in throat disorders, especially **acute** and **chronic pharyngitis** and mild **laryngitis.** Internally, the drug has been used in **gonorrhea, leucorrhea,** and **diarrhea,** especially of the serous type of the latter disorder. H.

GANGRENE.

GANGRENE.—**DEFINITION.**—This term is usually attributed to death or mortification of soft tissues, while the term "necrosis" is reserved for death of osseous or cartilaginous tissues.

VARIETIES.—Gangrene is divisible into several varieties: *moist gangrene,* due to arrest of the vascular supply, and in which the parts are soft and pulpy; *dry,* or *senile gangrene,* or mummification occurring in old age, in which the tissues become leather-like and wrinkled; *spontaneous gangrene,* a relatively rare form affecting the extremities and observed in apparently strong and young subjects; *ergot gangrene,* which occurs in individuals who, in consuming rye or rye bread, become exposed to ergot of rye; *diabetic gangrene,* which occurs as a complication of advanced diabetes; *pressure gangrene,* due to pressure and which occurs occasionally as a complication of bed-sores; and *symmetrical gangrene,* or Raynaud's disease, a paroxysmal form affecting mainly the tips of the fingers and toes.

SYMPTOMS.—The symptoms vary greatly according to the primary pathogenic factor and to a degree upon the location of the gangrenous process.

MOIST GANGRENE.—This variety is that most frequently met, owing to its frequent occurrence as a result of accidents, irreducible hernia, etc. Being due to arrest of the blood, both in the arteries and veins, there is softening, or liquefaction. The tissues assume various shades, varying from bluish green, red, to black; and blebs containing a very foul and fetid liquid are formed, the mortifying tissues giving off gases composed mainly of sulphide of hydrogen, ammonia, and volatile fatty acids. This form is likely to occur after severe injuries, such as crushing, burning, or even frost-bite. It is also observed when open wounds have been exposed to infection through imperfect or uncleanly dressings. A form of moist gangrene, also of traumatic origin, is sometimes witnessed after a large vascular trunk has been destroyed, which may spread with great rapidity.

In an average case the gangrenous area undergoes, as stated, a characteristic change of color. At first the boundary line between the dead tissues and the living ones is imperfectly marked. Where the progress of the necrotic process is arrested, however, through the vital resistance of the tissues, an area of inflammation interposes itself as a protecting wall, which becomes more or less perfect as the granulation tissue formed is healthy. This constitutes the *line of demarcation.* The inflammatory process continuing beyond, suppuration ensues, and the dead tissues may thus be entirely separated from the living ones through nature's efforts. The inflamed area is distinguishable from the healthy or gangrenous ones by its bright-red color, which changes to blue or black in the direction of the dead tissues. Unfortunately nature's efforts do not always succeed, and the morbid process may penetrate the limiting barrier, and invade the tissues beyond, extending gradually until death ensues.

The constitutional symptoms depend upon the amount of tissue involved. At first when an extremity is affected there may be but slight general disturbance; when, however, the gangrene ascends the limb, fever and other evidences of toxemia appear.

The extension of gangrene depends to a great degree upon the nature of the cause and the general health of the patient. An injury, which, through interruption of the circulation, is followed by gangrene, often remains circumscribed to the region in which the blood-flow has been reduced or arrested, provided, however, the general condition of the patient is favorable. Persons in poor health, or individuals who have lowered their vital powers by the excessive use of alcohol, overwork, insufficient food, etc., however, are much more exposed to extension of the gangrenous process.

Complications incident upon the destructive nature of gangrene usually lie behind a fatal issue, when this occurs. An artery may be eroded, giving rise to mortal hemorrhage; pyemia and septicemia through penetration into the blood of pyogenic micro-organisms or their toxins, peritonitis through extension of the gangrenous process from a gangrenous hernia, etc., may be mentioned among the many death-producing conditions which can appear.

In the cases previously alluded to, in which gangrene spreads with great rapidity, the so-called *traumatic gangrene,* the blood-supply is not only interrupted from an extremity, but there is septic infection besides. In a few hours in such cases the gangrene may have spread up an entire extremity through the agency of infectious bacteria. The skin becomes brownish red, black, or green; gas is rapidly formed, and the patient quickly succumbs to acute septicemia, unless amputation has promptly relieved him of the source of infection. The term "traumatic" is inapplicable to such cases, because it implies that this virulent form of the disease is to be expected after traumatism.

In truth, gangrene seldom occurs nowadays owing to modern methods, and, even in severe injuries of an extremity witnessed in the average hospital case, separation of the dead tissues soon occurs. Strict antisepsis in all surgical procedures adopted, greatly limits the likelihood that a dangerous form of gangrene will appear. Yet even slight exposure of a wound to infection may be followed in suitable environment by an active necrotic process endangering the life of the patient.

DRY GANGRENE.—In this variety of gangrene, of which senile gangrene is a type, there is a distinct absence of fluids, and the process of mortification is more a metamorphosis into an inorganic mass than a true decomposition; hence the term "mummification" frequently applied to this form. The local blood-supply gradually diminishes, the tissues shrink, become dark brown or black, wrinkled, and the skin becomes leathery. It usually affects the toes, sometimes the fingers, and may spread to the plantar or palmar surfaces.

SPONTANEOUS GANGRENE is rarely observed. It may be met with in subjects who apparently are in excellent health, but affected, as autopsies have shown, by arteriosclerosis. The arteries are narrowed, and thrombi are sometimes widely disseminated through the affected limb. (This is well shown in the annexed colored plate.) This renders spontaneous gangrene particularly malignant, and amputation of the limb is often necessary, preferably above the knee-joint, when the morbid process affects a leg. Unlike other varieties, it gives rise to acute suffering, owing to involvement of the local nervous supply, the principal branches of which are often found greatly thickened. Spontaneous resolution is rarely observed in this form.

> Fifteen cases of spontaneous gangrene of the legs in the puerperium. It may be due to embolism detached from a diseased heart-valve and lodged in the anterior tibial artery, or from arterial thrombosis extending from the placental site to the iliac vessels. The gangrene is usually dry, and the pain very severe, and forms a distinct line of demarcation. Diagnosis is established by severe pain, discoloration, coldness, with loss of sensibility in the part. Wormser (Centralbl. f. Gynäk, Jan. 26, 1901).

Among the forms of gangrene affecting the extremities, especially the lower ones, there is one of spontaneous origin occurring in the comparatively young. In such gangrene, the inner coat of the artery ordinarily, but occasionally of the vein, is found proliferated and thickened, thrombosis follows secondarily, the organization of the thrombus finally occluding the vessel. To distinguish between the proliferated inner coat and the organized thrombus, is to bear in mind that the former is composed of compact tissue, containing no elastic fibers and occasionally has hematin granules deposited within it. The thrombosis extends upward or downward from some point of the proliferated inner coat, or it arises at the very outset in several spots. The arterial sclerosis here does not differ from the ordinary arterial sclerosis. As probable causes of this condition may be mentioned predisposition, certain mechanical and chemical actions, and anything that tends to produce sclerosis. As to age, it is most common between 30 and 50, next between 30 and 40; the left side is more frequently affected than the right; it is also more common in the male than in the female. Kojima (Sei-I-Kwai Med. Jour., July 31, 1903).

In the literature the writers found 73 cases which they consider undoubted examples of spontaneous gangrene; 69 patients were males and 4 females; 2 patients were under 20 years old, 7 were between 20 and 30; 9 between 31 and 35; 22 between 36 and 40; 12 between 41 and 45; 10 between 46 and 50; 10 between 50 and 60; 1, age not mentioned. Although the symptoms in 1 case were present for over twenty years, the average duration was from three to five years. In the 68 cases in which the location was mentioned, the condition occurred 53 times in the legs alone, twice in the arms alone, and 13 times in both upper and lower extremities. In more than one-third of the cases the pulse in the femoral and all the vessels distal to it were lessened or obliterated, while in nearly two-thirds the vessels as high as the popliteal were involved. Neither syphilis nor the use of tobacco seemed to play any part in the causation of this condition. The authors report 1 case seen by them. They believe that it was a case of general arterial thrombosis, exactly similar to that found in the extremities in the condition known as spontaneous gangrene. Dexter and Ellis (Cleveland Med. Jour., Aug., 1910).

ERGOT GANGRENE is also partly of neurotic origin, the main pathological factor being vasomotor spasm brought on by the ingestion of ergot of rye when rye flour is used instead of wheat flour in making bread, as is the case in many parts of Europe. The continued consumption of ergot of rye gives rise to various preliminary symptoms: general adynamia, gastric disorders, formication, and fugitive pains. The arrest of the blood-current through the spasmodically contracted arteries is soon followed by blanching and lowered nutrition, which makes the part vulnerable to the least traumatism. Even without such, the ill-nourished areas farthest from the center—the toes, the ears, the nose, etc.—finally succumb.

DIABETIC GANGRENE.—Gangrene is rather frequently observed in diabetics, especially in persons advanced in years. (See also the article on DIABETES, this volume.) Heidenhain attributes it to the common cause of senile gangrene, arteriosclerosis; the main factor he believes to be an abnormal susceptibility to wound infection. Still, the fact that internal viscera sometimes become gangrenous in such cases would tend to invalidate this view. In a case witnessed by Turner the pyramids of the left kidneys were found gangrenous. A marked line of separation existed, and every other portion of the organ was healthy, as was also the entire urinary system.

Hyperglycemia is not a very important factor in the induction of the gangrene, but looms into importance after gangrene has been established in so far that it invites septic infection and encourages the occurrence of the three acid bodies occurring in diabetes. Acetone has a very low degree of toxicity, and probably does not contribute to the production of gangrene. Diacetic acid is always to be looked upon as a pathological agent, though of itself not very harmful and indicates that betaoxybutyric acid is being oxidized. Betaoxybutyric acid, when present in the urine, is to be viewed as the special chemical agent fostering gangrene, which, however, is ineffectual in bringing about that result if acting alone in the absence of arteriocapillary sclerosis. The quantitative ammonia excretion is the expression of measure of the amount of unburned betaoxybutyric acid. It is not an accurate standard of measurement, always registering too little. The excretion of 1 Gm. in twenty-four hours is to be looked upon as contraindicating operation except in great emergency. Eising (Med. Rec., Aug. 15, 1908).

PRESSURE GANGRENE.—This occurs when a region in a low state of vitality—such as occurs in prolonged fevers, etc.—is submitted to continued pressure. The vascular supply, already weakened, becomes further weakened, especially when, as is the case over the sacrum, the scapula, etc., the soft tissues are pinched, as it were, between a bone and the bed. The slightest injury over such a site becomes the seat of ulceration, the so-called "bed-sores," and gangrene is apt to follow, if through the presence of arteriosclerosis and old age the lumen of the vessels is already limited.

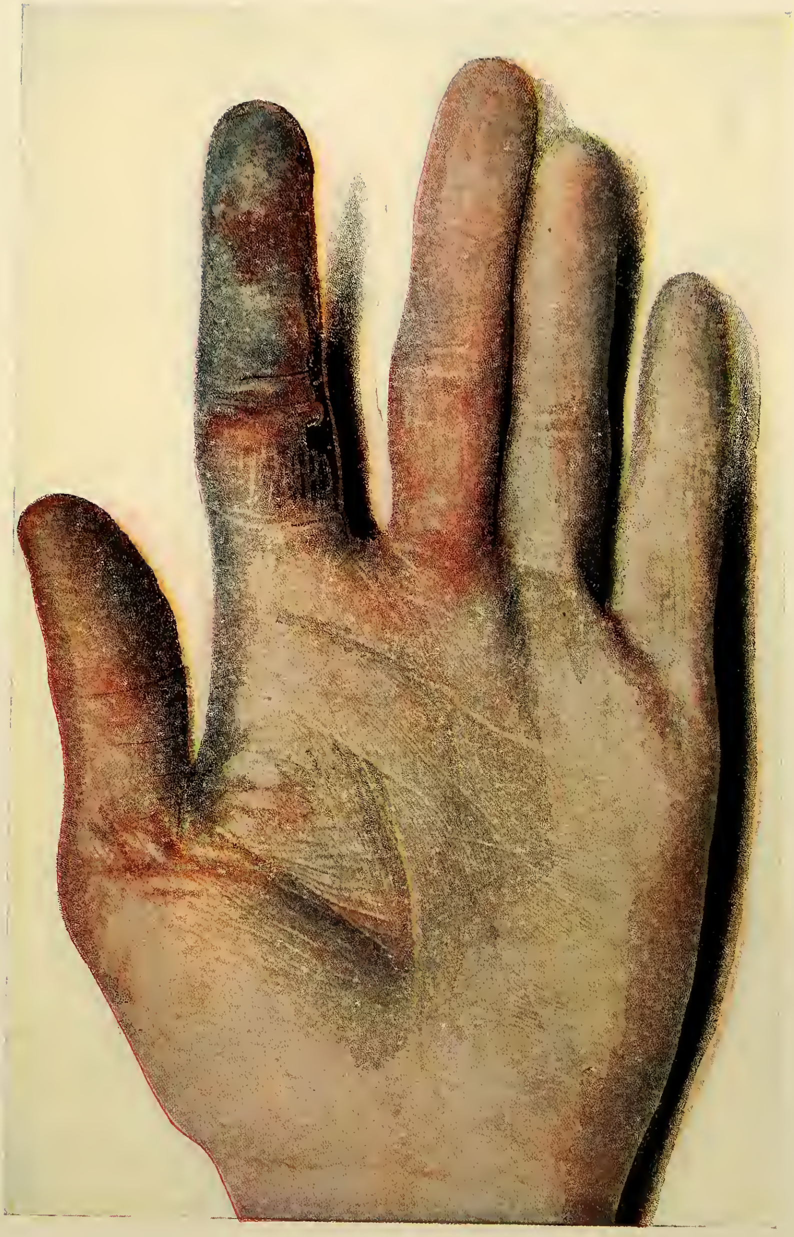
SYMMETRICAL GANGRENE, or Raynaud's disease, is a form which occurs in paroxysms. It begins with paresthesia and sharp pains. The tips of the fingers and toes, the parts most frequently affected, then become cyanotic and gangrenous. The entire phalanx is occasionally involved. It is occasionally observed in other parts of the body, the unaffected surfaces being usually very pale.

Case of symmetrical gangrene following local asphyxia in the tips of both ears. This localization is regarded as rare, from the fact that Raynaud, in his description of the condition which bears his name, makes no mention of such lesions occurring about the face save in one instance in which small cicatrices were seen by him about the nose, though the disease itself had not been observed in this location. In the author's case, anemia seemed to enter largely into the etiology of the affection, as in Hochenezz's, Rham's, and Steiner's cases. Canessa (Revista medica del Uruguay, Yr. vi, No. 4, 1903).

CARBOLIC ACID GANGRENE.—Carbolic acid has caused gangrene in so many cases that it seems to merit a special place among chemical agents capable of inducing this condition. Even in 2 per cent. solution, this agent is capable of destroying the life of tissues. The majority of cases reported in which gangrene occurs were felons or slight disorders of the finger-tips or toes. According to Czerny the duration of the application is more important than the strength of the solution, the anesthetic action of the drug causing it to be left *in situ* prolonged periods at a time. The parts first become grayish white and eventually black. There is no pain, and the gangrene is only revealed by the appearance and the stiffness of the finger or toe affected.

Eighteen cases of gangrene of the fingers, the result of weak carbolic acid dressings. This makes a total of 132 cases reported. Carbolic acid in any strength as a moist dressing is dangerous, and should never be used. F. B. Harrington (Amer. Jour. Med. Sci., July, 1900).

Nine cases of gangrene of the finger or fingers, due to the application of carbolic acid dressings. In 7 out of the 9 cases, amputation was required. In 4 of the cases the strength of the solution used was not over 5 per cent. In none was a waterproof covering used, nor had there been any constriction by a bandage. The appearance of the gangrenous part is characteristic. The skin is at first dry, wrinkled, and grayish white in color; later it becomes darker and more shrivelled. At the junction of the living and dead tissue there is some hyperemia, and eventually a line of demarcation forms. This should always be waited for before amputation is performed. Wallace Brit. Med. Jour., May 11, 1907).



Carbolic Acid Gangrene of Finger. *(Jas. A. Kelly.)*

Annals of Surgery

Case of carbolic acid gangrene in a woman, aged 27, who applied a solution of carbolic acid (strength unknown) to a punctured wound of the finger. The dressing remained in place from 11 P.M. till 4 A.M., when it was removed on account of intense pain. The writer advised the patient to have the finger amputated, but she refused. Subsequently she went to another hospital, where the finger was amputated at the metatarsophalangeal joint. Kelly (Annals of Surg., Feb., 1909).

The writer condemns the sale of carbolic acid to the public, warns the physicians who use carbolic acid in the form of moist compresses that unpleasant results not infrequently follow its use, and suggests a new factor, possibly two, in the production of carbolic acid gangrene of the fingers and toes. He cites 4 cases of carbolic acid gangrene and presents the two following factors as hitherto unrecognized ones: 1. The mechanical constriction to the circulation, due to the contracted and hardened skin, which acts like a tight bandage applied to the part. 2. The possibility of a sclerotic artery, which is not uncommon in the young, playing a part in some of these cases, as it undoubtedly did in the case which he describes. Leighton (St. Louis Med. Rev., Feb., 1909).

Case of an elderly man who, for a slight bruise and abrasion due to a railway accident, applied an ordinary phenolized petrolatum. After a few applications the tissues broke down into a progressively enlarging gangrenous ulcer, the lesion being upon the leg two inches below the patella. It was cleaned out and treated with hydrogen peroxide and tincture of iodine; healed but again broke down, and now indicated malignancy. At the end of several months' treatment, X-ray applications finally caused healing. E. Buckmaster (Jour. Amer. Med. Assoc., Jan. 13, 1912).

ETIOLOGY AND PATHOLOGY.—The causes of tissue-death are divided by Tillmann ("Surgical Pathology," Rogers's transl.) into four general classes: 1. Interruption of the afferent flow of arterial blood without the development of a collateral circulation, such as may occur in the cases of thrombosis and embolism, or after ligation, or in consequence of the pressure of a tumor or inflammatory exudate. 2. Interruption of the efferent flow of venous blood. 3. Interruption or stasis of the circulation in the capillary walls. 4. Death of the tissue-cells without any disturbance of circulation, due to poison, such as snake-bites, or to micro-organisms or the products of their metabolism, such as are found in infectious diseases of wounds; for example, erysipelas, cellulitis, and septicemia and finally to local anesthesia.

The writer observed 2 cases of gangrene after local anesthesia; in 1 the great toe became gangrenous four days after an operation under local anesthesia for an ingrowing nail. In the other case a hydrocele was operated on under novocaine-adrenalin and gangrene of the scrotum developed. Both patients were elderly and there was a suspicion of arteriosclerosis. A salt solution used was unusually strong, owing to a mistake, and experiments with this solution showed that the addition of the adrenalin favored the production of gangrene. The writer warns that the salt solution should never be stronger than 0.9 per cent., approximately the same osmotic tension as that of the blood proper. Strohe (Deut. Zeit. für Chir., July, 1909).

Local and general anemia, venous stasis, disturbances of circulation from diseases of the vessels,—heart or lungs,—or disturbances of circulation due to inflammation—in short, faulty circulation from any cause—increase the disposition to gangrene from the effects of chemical or thermal influences.

The special etiological factors have been already alluded to, while gangrene as a complication of various infectious diseases has been reviewed in the respective articles upon the latter.

Study of 15 specimens of gangrene. In cases due to arterial sclerosis a high-grade sclerotic proliferation of the intima is found, causing stenosis of the lumen of one or more of the main vessels. It threatens the life of the extremity by closing the exit of the branches from the vessel involved, preventing the formation of collateral circulation. A secondary progressive thrombosis is also apt to develop on the changed arterial wall. Senile or diabetic gangrene, a localized petrifaction of the arteries, sometimes forms. Bunge (Archiv f. klin. Chir., Bd. lxii, H. 1, 1901).

Analysis of personal cases and of all the cases of gangrene following infectious disease found in literature: 166 in all. The most frequent causes were typhoid and typhus fever, and after these influenza, puerperium, and pneumonia, in the order named. Scarlet fever was the cause in only 3 cases, and diphtheria in only 1. The commonest seat is in the legs, 122 cases having gangrene in this situation. There appears to be no difference between the right and left legs, and gangrene of both legs is less common than of either separately. In 128 cases of which the result is known, 42 patients died. The percentage is much higher among women than among men. In 65 cases autopsy showed thrombosis in the main artery of the limb. In many of the others investigation was not made. Eichhorst (Deutsches Archiv f. klin. Med., vol. lxx, H. 5-6, 1901).

Rapidly spreading gangrene, the *gangrène foudroyante* of French surgeons, is developed when to a necrotic process in the economy there is added a rapidly spreading emphysematous condition of the surrounding parts, with increased tension, crepitation, the formation of gaseous bullæ, and a bronzed and streaky discoloration of the skin. The disease, once established, tends to spread rapidly to other parts of the body, and constitutes the most fatal form of gangrene.

Gaseous gangrene may be produced by various micro-organisms, particularly, however, by the *Bacillus aërogenes capsulatus,* which, without having a specific action, behaves in man as a toxin saprophyte upon tissues already seriously damaged. The *Bacillus coli communis,* with other germs, may also cause gaseous gangrene. Muscatello (Rif. Medica, May 21, 22, 23, 1900).

Case of gaseous gangrene in a non-diabetic person, in which the bacterium coli was the sole agent isolated. This germ cannot, however, produce gaseous gangrene alone; its action is then entirely saprophytic and is dependent upon other pathogenic organisms, or upon local or general nutritional disturbances, such as trauma and metabolic diseases. Dansauer (Münch. med. Woch., Sept. 8, 1903).

Infectious gangrene of the skin is occasionally observed. According to Caillaud this appears under two conditions: There may be a previous ulcerative skin-lesion, from and upon which the gangrene starts, or the gangrene may appear immediately after a non-ulcerative manifestation of the skin; it is not an occasional accident, but constitutes an essential element of the disease. Any cause which impairs general health predisposes to that contagious affection, and existing ulcerations and erosions serve as a door of entrance for the contagion.

Case of a little girl, aged 19 months, who was suddenly taken ill with vomiting, diarrhea, tenesmus, fever, and convulsions. On the following day a small blister was found on the right nate. This spread rapidly until it covered the right buttock, extending to the left. There appeared four blisters on the back and one on the thumb of the right hand. These blisters increased in size considerably, became dark red in color, livid in the center. The patient died on the third day. Smith (Jour. Kans. Med. Soc., Feb., 1907).

Spreading traumatic gangrene, though usually developed in subjects suffering from general depraved health, occasionally occurs in healthy subjects through infection of the wound by the anaërobic bacilius of malignant edema of animals, and to which fowls are particularly susceptible. Through the experimental observations of Chauveau and Arloing, Brieger, Ehrlich, and others, the fact has been practically established that the same germ, which, on the one hand, may give rise in animals to malignant edema, may, on the other, when ingrafted in man on tissue the seat of a moist gangrene, produce the emphysematous condition.

In the field-mouse, an animal immune to the bacillus of septicemia, Koch has produced, experimentally, a progressive gangrene from inoculations with chain micrococci not to be distinguished from the *Streptococcus pyogenes*. He has also shown that the ptomainic products of bacterial activity may themselves cause the destruction of tissue, since, in the examination of specimens from the inoculated animals, the progressive necrosis was observed markedly in advance of the bacterial invasion.

Case of gaseous gangrene complicating a compound fracture of the right forearm in a boy of 10 years, the bones coming in contact with mud. For the first two days the patient did well, then the arm began to swell and became rapidly emphysematous and gangrenous, with a line of demarcation an inch above the elbow; the swelling was dusky in color and there was crepitation extending over the scapula and below the clavicle. Several long incisions were made along the forearm and gas escaped with great force. Antiseptic measures were carried out and the condition of the arm rapidly improved, probably because of the relief from pressure on the blood-vessels by the gas. Amputation at the junction of the upper and middle third of the arm was necessary, however. The condition is believed to have resulted from infection with the *Bacillus aërogenes capsulatus*, but no bacteriological examination is reported. Reports of 16 cases of infection by this micro-organism in literature, with 12 deaths and 4 recoveries found. C. P. Gildersleeve (Med. Record, March 4, 1899).

Study of the nature of the vascular lesions observed in 14 cases of senile and diabetic gangrene. There is most probably a primary arteriosclerosis obliterans which terminates in thrombosis; the latter extends into the collateral branches, abolishes the anastomotic circulation, and determines the occurrence of gangrene. Bunge (Edinburgh Med. Jour., Sept., 1900).

TREATMENT.—Removal of the causative factors and especially those interfering with free circulation is the first indication. In strangulated hernia, section of the constricting ring brings about this result; in paraphimosis, pressure from superficial tumors, bed-sores, tight bandages, etc., relief can be afforded also by overcoming the constriction. In many cases, however, this is not possible. In obstruction due to thrombosis and arteriosclerosis, for example, everything should be done to facilitate the return of the blood by judicious procedures. In purely thrombotic cases, **hypodermocylsis,** or intravenous infusion of **saline solution** to increase the fluidity of the blood may prove useful. **Elevation** of the **part,** with **slight flexion** of the **extremity** affected, gentle **massage** toward the heart, **warmth,** taking care to avoid "hot-bottle burns," which under such circumstances are easily inflicted, represent the minor indications.

Amputation, the sole effective measure hitherto available in dealing with cases of diabetic gangrene due to obliteration of the arterial supply, is itself attended with danger, the organism already being placed in jeopardy because of the absorption of toxins. Dieulafoy recently found that by employing currents of **air heated** to 150°, 300°, 500° C. or even higher, extension of the gangrene and toxic absorption could both be arrested. On repeated use, such currents produce carbonization of the part and limit the gangrenous process by keeping the tissues dry. Extension of the process and infection having been checked, **amputation** can with safety be performed and the patient rid of the necrosed segment of limb. Marked success was obtained in the cases thus treated.

Case of a man 64 years old, diabetic for years, who had lost in the past eighteen months about fifty pounds. The trouble began with violent pain in the left leg, and inside of forty-eight hours gangrene had set in in the entire region below the garter. The urine showed 82 Gm. of sugar for twenty-four hours with albumin and acetone. **Hot air** treatment was begun at once and continued twice a day half an hour at a time—air at 300° C. on the portion below the separation line, at 80° to 100° on the living tissues above the line. The patient began to improve at once. The sugar decreased steadily, the acetone also; the temperature of the air-douche was raised to 400°. The leg mummified. Gradually a deep line of separation formed at the garter, which was followed up closely by the **hot-air douche,** and finally all the posterior tissues separated spontaneously, leaving the bones bare. Dieulafoy (Bull. méd., Feb. 16, 1910).

In the obstetrical tears which suppurate and show tendency to gangrene, the writer has obtained excellent results by application of **superheated air;** it penetrates into all the infected crevices and destroys the putrefying tissues while inducing a reparative hyperemia in the surrounding tissues. In 1 of the 3 cases reported in detail this aërothermotherapy rapidly arrested the gangrenous process in the cervix and the development of the threatened vesicovaginal fistula was checked. Dupont (Annales de gynec. et d'obstet., July, 1910).

When, notwithstanding prophylactic measures, the gangrenous process develops, disinfection of the area should at once begin. **Iodoform, orthoform, aristol,** and **resorcin** are valuable in this connection.

Remarkable results obtained in a diabetic who had had gangrene in one leg which necessitated amputation. The other leg became involved, and a succession of scabs formed on the foot. No pulse could be felt in the dorsal artery of the latter or in the posterior tibial. After a half-hour's **massage** the whole foot and leg were warmer, the tissues softer, and the tension less, and the dorsal artery could be felt so that the pulse could be counted. The method of work was principally by deep manipulation in a downward direction to aid the arterial current, followed by upward friction, or effleurage, to aid the venous and lymphatic flow. Douglas Graham (Inter. Clinics, vol. iv, series 10, 1901).

The next object is to prevent infection of the healthy tissues beyond by products of decomposition. Any accumulation of offensive fluid or gas should be prevented by evacuating foci and treating the part with antiseptic lotions. An excellent agent in this connection is **permanganate of potassium** in 1-grain-to-the-ounce solution. Infiltration abscesses should be followed up to the living tissues above, if needed, to thoroughly clear them of the infecting elements. Carbolic acid should not be used as a disinfectant, since it tends to lower the vital resistance of the tissues and to promote gangrene.

In severe wounds of the extremities in which gangrene is threatened, as evidenced by cyanosis and coldness of the distal part, the author believes that the gangrene results from stasis of the blood. In order to promote the circulation, he recommends one or more small **incisions in the cyanosed area,** application of a **camphor-oil dressing** (to prevent drying), and placing the extremity in a **suction apparatus** at a negative pressure of between 12 to 15 cm. for eight to ten minutes. This is done two or three times a day for a week. It will be noticed that arterial blood exudes which increases in quantity day by day. The color slowly improves, the sensibility of the part returns, and the wound heals nicely. In a number of cases the writer believes that he has saved portions of an extremity which would otherwise have become lost. H. Noesske (Centralbl. f. Chir., Oct. 2, 1909).

Case which confirms anew the great value of stimulating the capillary circulation by **Noesske's method** of cutting down to the bone at the tip of the finger parallel with the nail. Fehsenfeld (Münch. med. Woch., Oct. 29, 1912).

The adoption of radical measures must be regulated by the progress of the case and the nature of the primary disorder present.

In a case of diffuse phlegmon of the leg with gangrene the writer used successfully: 1. Linear applications of **thermocautery.** 2. Subcutaneous injections of **hydrogen peroxide** 1 to 2 centimeters above infected area. 3. **Passive hyperemia** induced thrice daily by rubber bandage above knee. 4. Daily bathing of part in warm **permanganate** solution 5. Wet dressing of hydrogen peroxide. H. Petit (Arch. de méd. militaire, No. 12, 1909).

Arteriovenous anastomosis has been tried by Hubbard with improvement as result. The measure has not been applied with sufficient frequency to render a verdict as to its value possible. . . .

> Case in which the circulation in the foot was sufficiently improved by the operation so that the color of the area, originally purple, changed and became almost normal in appearance, with the exception of the toes. Edema of the leg, which was slight at first, became excessive. It made the leg seem stiff and full to the patient. Coincident with the appearance of this edema, pain, which had decreased since the operation, returned, and from that time on became the most prominent symptom. Hubbard (Boston Med. and Surg. Jour., Oct. 7, 1909).

> Series of 4 cases of senile gangrene in which the writer tried **anastomosis between the femoral artery and vein.** No benefit was observed, the lesions being too far advanced. The reduced blood-pressure and the atheromatous state of the internal wall of the artery explain the failure of such operations for senile gangrene. To have any chances of success they should be done early in the course of a case. Mauclaire (Arch. gén. de chir., Aug. 25, 1913).

It is generally thought advisable not to interfere with the reparative efforts of nature when the line of demarcation is clearly established. When, however, in the case of an extremity, there is no line and the morbid process ascends here and there or evenly and the patient shows evidences of impending constitutional disturbances, the question of **amputation** is in order. In arriving at a decision in this connection the various reasons for an amputation should be carefully computed, namely: The nature of the causative disorder; the probabilities as to spontaneous resolution; the subsequent deformity involved, both without and with amputation based upon the parts (muscles, nerves, vessels) already destroyed; and last, but not least, the general health of the patient. These may all prove useful in case of subsequent controversy. Severe injuries followed by gangrene warrant amputation if the tendency to spread is evident. When a putrescent mass, however, though the line of demarcation be present, exposes the patient to general toxemia, amputation is also warranted as soon as the signs of septicemia appear. Especially is this true in "traumatic gangrene."

All surgeons agree that a high amputation is to be preferred, and the knee or thigh is usually selected because the profunda femoris is rarely obstructed by thrombi.

When **amputation** is determined upon, the anatomical distribution of the vascular supply of the part must clearly be borne in mind and an effort made to leave in the flaps, not only unobstructed vessels, if arteriosclerosis or thrombosis be present, but also a sufficient supply to insure proper nutrition.

> We possess no means of establishing at what level the vessels of the leg are in a healthy state, *i.e.,* where to amputate. In order to determine the state of the vessels, the writer recommends that the affected leg be rendered bloodless by means of an Esmarch bandage, and that the bandage then be suddenly removed. In a healthy leg sudden removal of this sort is followed by an active red hyperemia extending to the tip of the toes, whereas, if the vessels are diseased, the hyperemia occurs more slowly and usually extends only as far as that point where the vessels are in good condition. The writer quotes 3 cases in which amputated legs were studied with the result that the preoperative diagnosis was absolutely confirmed. A. Moszkowicz (Mitt. a d. Grenz. d. med. u. chir., Bd. xvii, H. 1 u. 2, 1908).

Smith recommends the following amputation when gangrene of the foot is present, and when it is decided to amputate at the knee or through the thigh. There being eight arterial branches in this region, if the incisions and flaps are suitably planned this arterial supply need not be seriously interfered with. His method of amputation is as follows: A straight incision is made from two inches above the upper border of the patella downward over the center of that bone to the tuberosity of the tibia. From the lower extremity of this perpendicular incision two curved incisions are made, having their convexity downward, and extending, respectively, in the direction of the external and internal borders of the limb. These two incisions having been united posteriorly by a straight incision across the upper border of the calf, the flaps are dissected up from the tibia and fibula, the patella is removed, and the knee-joint is disarticulated.

In *senile gangrene* a conservative line of treatment is indicated, since meddlesome surgery here is liable to be followed by extension of the morbid process. Attention to the healthy tissues of the entire surface is necessary, since a minute abrasion, a slight blow, may become a gangrenous area. As taught by Jones, when the gangrene affects one or two toes and the patient's condition is satisfactory, the surgeon should be content with the expectant plan of treatment, taking precautions to lessen or prevent the effects of local septic infection. When, however, the gangrene has reached the metatarsus, he should be prepared to perform the high operation; that is, **amputation** above the knee.

The local treatment in limited forms of gangrene should consist in thorough cleansing of the foot and leg, free dusting of the immediate vicinity of the dead part with **iodoform,** and the application over this powder of **sublimate** or **salicylic wool.** The use of artificial heat in the form of poultices and fomentations is positively mischievous. Pain may be relieved by the internal administration of **opium** and the local application of a powder composed of **boric acid, sublimate of bismuth,** and **hydrochlorate of morphine.**

> Case of synchronous **amputation** of both thighs for gangrene of the feet under special cocainization. The patient was a man of 68 years. Twenty minims of 2 per cent. solution of **cocaine hydrochlorate** were employed, the needle being entered between the fourth and fifth lumbar vertebræ. The result was in every way satisfactory. G. G. Hopkins (Amer. Medicine, June 15, 1901).

In the treatment of *diabetic gangrene* no special features are indicated. Heidenhain, who has given the subject special attention, states that, as in senile gangrene, as long as the gangrene is confined to one or two toes the line of demarcation should be awaited and the dead tissues allowed to separate of themselves. Removal of the gangrenous portion with forceps and scissors may lead to gangrene of the parts above, although the line of demarcation has been fully established. As soon, however, as the gangrene attacks the sole or the dorsum of the foot, an **amputation** of the thigh should be made as close above the condyles as possible. Amputation below the knee is nearly always followed by gangrene of the flaps.

In 11 cases of diabetic gangrene 6 were saved by thigh amputation; 2 of the 3 fatal cases had large quantities of sugar in the urine (8 per cent. and 5 per cent.), while the remaining 2 showed much albumin in addition to sugar. Such cases should avoid even insignificant injuries, which in them may assume serious proportions—precisely as in senile gangrene.

Symmetrical gangrene rarely calls for surgical interference. The treatment of the neurosis and constitutional measures are generally sufficient, and has been described elsewhere.

CONSTITUTIONAL MEASURES.—These should not be neglected. Nutrition should receive especial care, and the patient should be supplied with nourishing food. The low **diet** which older ideas seemed to warrant belongs to the past. **Alcoholic stimulants** should be given, but in small quantities at a time—just enough to sustain normal cardiac action. **Strychnine** is a valuable adjuvant, by stimulating vasomotor action. Promiscuous drugging should be avoided. **Hypodermoclysis,** or, better, **saline solution** intravenously are, however, rational measures, their purpose being to increase the fluidity of the blood.

GANGRENE DUE TO SYPHILITIC ENDARTERITIS.—Lesions in the blood-vessels in the secondary period of syphilis are, according to Ravogli, the result of a hyperplastic inflammatory process, and in the tertiary period represent a true gummatous infiltration. It is now clear that the spirochetes circulating free in the blood attack the epithelial lining of the vessels, causing alterations in them. Several observers have found spirochetes in large colonies in the vascular tunics. The organisms have also been detected in the superficial network of inflamed capillaries. In the arteries the adventitia is scarcely distinguishable from the other tunics, the media appears smaller and compressed, while the intima is thickened and interwoven with hyperplastic young cellular elements concentrically disposed. The lumen of the artery is diminished and altered in shape; often it is occluded by a thrombus. According to the vessels involved three forms of gangrene may be produced: 1. *En masse,* when the principal artery of a limb is occluded, oftenest due to endarteritis in the late stage of syphilis. 2. Superficial, the result of an acute endoangeitis in the small arteries supplying an area of skin. 3. In the center of deep syphilitic lesions, due to pressure of the infiltrating elements on the blood-vessels and tissues.

> Three cases of syphilitic gangrene. In the first, gangrene began in the toes and spread upward to the whole foot, malleoli, and knee. On amputating at the thigh, the femoral artery was found rigid and occluded by a thrombus. The gangrene continued and death occurred from sepsis. The second case presented a superficial gangrenous condition of the external region of the whole left thigh, extending to the upper third of the leg. Sloughing took place after a few days of local treatment (continuous baths of 1:10,000 **bichloride of mercury**), and the area gradually healed. In the third case, a gumma of the lower lip developed into an extensive gangrenous mass, further progress of which was arrested by deep injections of 1 per cent. **bichloride of mercury** solution, large doses of **potassium iodide**, and locally a moist dressing of 1:5000 **bichloride**. The surface healed, leaving a bad scar, which was corrected by a plastic operation. Heroic antisyphilitic treatment is necessary in these cases, the gangrenous process having been checked thereby in several instances. Especially when the syphilitic process has acted on the small vessels can limitation of the gangrene be obtained. In all the cases tonic treatment, particularly **quinine** in large doses, was found of great value in subduing septic conditions. A. Ravogli (Lancet-Clinic, Feb. 12, 1910).

It is probable that **salvarsan** will prove efficient in these cases, though literature does not seem, at the present writing, to contain instances in which this remedy has been tried to curtail the gangrenous process. S.

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